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20 Victoria Street
Toronto, Ontario M5C 2N8
Tel.: (416) 362-5211
Toll Free: 1-800-387-2689
Fax: (416) 362-6161
Email: info@micromedia.on.ca

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Ontario Guidelines for the Management of Anxiety Disorders in Primary Care

Ontario Program for Optimal Therapeutics

Guide To The Guideline

Differentiating Among the Anxiety Disorders [1]

PHOBIC GROUP

Panic Disorder with or without Agoraphobia	• Sudden, recurrent episodes of intense anxiety or panic attacks that occur "out of the blue", with no situational trigger • Focus of anxiety is often expectation of having another attack • Wide range of physical symptoms occur • With or without agoraphobia, the fear of being in situations where a panic attack is likely to occur	**Page 23**
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Specific Phobia	• Fear of specific things (e.g., spiders) • Fear of specific situations (e.g., flying, elevators, heights) • May experience panic attacks when encountering phobic stimulus	**Page 29**

WORRYING GROUP

Generalized Anxiety Disorder (GAD)	• Uncontrollable and excessive worry about day-to-day normal life circumstances (e.g., finances, work, relationships), and improbable events • Worry often occurs on most days, over a long period of time (at least 6 months)	**Page 30**

TRAUMA AND STRESS RELATED

Post-Traumatic Stress Disorder	• Transient anxiety involving intense fear, helplessness or horror in response to a traumatic event (e.g., combat, abuse, natural disaster) • Symptoms: nightmares, flashbacks, intrusive memories, avoidance • Duration is more than 1 month • May experience panic attacks when exposed to trigger • **Acute Stress Disorder:** Symptoms develop within 4 weeks of event and last no longer than 1 month	**Page 32**

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Obsessive-Compulsive Disorder	• Presence of recurrent, unwanted thoughts, images or urges (**obsessions**) associated with compulsive, repetitive rituals (**compulsions**) in an attempt to reduce the related anxiety (e.g., fear of contamination causing repeated hand washing) • The anxiety is generally not about an everyday concern	**Page 35**

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Ontario Guidelines for the Management of Anxiety Disorders in Primary Care

Anxiety Review Panel

September, 2000

For additional copies please write or call:

PUBLICATIONS ONTARIO
50 Grosvenor St.
Toronto, Ontario M7A 1N8
Telephone: (416)-326-5300 or toll-free in Ontario 1-800-668-9938.
Hearing impaired call: (416)-965-5130 or toll-free in Ontario 1-800-268-7095
Fax: (416)-326-5317

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Inclusion of a pharmaceutical product in these guidelines was determined solely on the basis of the Review Panel's expert professional assessment of the available evidence. It is not intended, and cannot be taken, as a recommendation that the product be included in the reimbursement policies of any drug plan or benefits manager.

Stakeholder groups were invited to participate in the development of these guidelines by reviewing and commenting upon the guidelines in draft form. These included health care professionals, professional societies, the pharmaceutical industry and the Ontario Ministry of Health and Long-Term Care.

Comments: A form is provided at the end of the document for the submission of reader's suggestions.

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TABLE OF CONTENTS

Page Number

Section I: Preamble 1
- Anxiety Review Panel 3
- Guideline Development Process 6
- Criteria for Level of Evidence and Treatment Assignment 7

Section II: Introduction 9
- Anxiety Disorders in Primary Care 11
- Differentiating Among the Anxiety Disorders 12
- Assessment Summary 13
- Treatment Summary 15

Section III: Anxiety Disorders and Therapies 21
- Panic Disorder with or without Agoraphobia 23
- Social Phobia or Social Anxiety Disorder 27
- Specific (formerly Simple) Phobia 29
- Generalized Anxiety Disorder 30
- Post-Traumatic Stress Disorder (PTSD) 32
- Obsessive-Compulsive Disorder 35

Appendices 37

Appendix A
- Red Flags for Detection of Anxiety Disorders in Primary Care 39

Appendix B
- Treatment Algorithm 40

Appendix C
- Cognitive-Behaviour Therapy (CBT) Terms 42

Appendix D
- Criteria for Diagnosis of Anxiety Disorders 44

Appendix E
Pharmacotherapy
- Anxiolytic Summary 51
  - Therapeutic Tips for Using Benzodiazepines 51
  - Management of Benzodiazepine Withdrawal 52
  - Benzodiazepine Equivalence Chart 53
  - Management of High Dose Withdrawal 54
- Antidepressant Summary 55
  - Switching Antidepressants 56
  - Frequency of Adverse Reactions to Antidepressants 58

Appendix F Consumer and Self-help Reading List 60

Appendix G Practice Treatment Manuals for Clinicians 62

Appendix H Video Resources 64

Appendix I Anxiety Related Associations 65

Appendix J Internet Resources 66

Reference List 69

Comment Sheet 83

Section I

Preamble

The Anxiety Review Panel

The panel represents a mix of health professionals with expertise in several fields and who practice in a variety of clinical settings. The panel was co-chaired by:

Dr. Jacques Bradwejn
Chairman of Psychiatry
Medicine
Faculty of Medicine
University of Ottawa

Dr. Michael Evans
Department of Family and Community
Faculty of Medicine
University of Toronto

Coordinator Research and Scientific Staff
Laurie Dunn MSc., BSc.Phm.

Dr. Martin M. Antony
Director,
Anxiety Treatment and Research Centre
St. Joseph's Hospital, Hamilton
Psychiatry and Behavioural
Neurosciences, McMaster University,
Hamilton

Dr. Peggy Richter
Anxiety Disorder Clinic
Centre for Addiction and Mental Health
Clarke Division
University of Toronto, Toronto

Dr. Diana Koszycki
Stress and Anxiety Clinic
Royal Ottawa Hospital
University of Ottawa, Ottawa

Marnie Shepherd
Coordinator
Consumer/Survivor Development Initiative
Toronto

Dr. Frank Jarrett
Psychiatry
Queen's University, Kingston

Dr. Richard Swinson
Chair of Psychiatry & Behavioural
Neurosciences
McMaster University, Hamilton

Dr. Ernie McCrank
Director-Anxiety Disorders Program
Royal Ottawa Hospital
University of Ottawa, Ottawa

Dr. Tom Ungar
Psychiatry
North York General Hospital
Psychiatry, and Family and Community
Medicine
University of Toronto, Toronto

Dr. Phil McGuire
Family Medicine
University of Ottawa, Ottawa

Dr. Lynn Wilson
Family and Community Medicine
University of Toronto, Toronto

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1. Ontario Anti-infective Review Panel. Anti-infective guidelines for Community-acquired Infections. Toronto: Queen's Printer of Ontario: 1997.
2. Canadian Respiratory Review Panel. Guidelines for the treatment of COPD. Toronto: MUMS/OTI: 1998.

Expert Reviewers

Dr. David Bakish *
Head
Psychopharmacology Unit
Institute of Mental Health Research
Royal Ottawa Hospital, Ottawa, Ontario

Dr. Murray Enns
Psychiatric Centre
University of Manitoba, Winnipeg, Manitoba

Dr. David Gardner
Department of Psychiatry and
College of Pharmacy
Dalhousie University, Halifax, Nova Scotia

Dr. Stanley Kutcher *
Professor and Head,
Department of Psychiatry,
Dalhousie University, Halifax, Nova Scotia

Dr. Jean-Michel Le Mellédo
Psychopharmacology Research Unit,
University of Alberta, Edmonton, Alberta

Dr. Jacques Plamondon *
Head
Anxiety Disorders clinic
Centre Hospitalier Universitaire de Quebec
Pavillon CHUL, Quebec

* Members of CANMAT (Canadian Network for Mood and Anxiety Treatments)

Special thanks to:

Caryn Thompson, Department of Family and Community Medicine, Faculty of Medicine, University of Toronto

Doctor of Pharmacy candidates Lori MacCallum, Jennifer Mather, Stephanie Tsao and Monique Zamin from the Faculty of Pharmacy, University of Toronto and Lilly Cheng, Faculty of Pharmacy, University of British Columbia.

Rhiannon Babineau, Elizabeth Coyle, Maria D'Angelica, John Pilla, Elise Sawatzky from Medication Use Management Services (MUMS) Inc.

Guideline Reviewers

Many thanks to the individuals below who carefully reviewed the guidelines and provided suggestions to help improve the document.

Canadian

Dr. Barbara Boyd
Family Medicine
Toronto, Ontario

Dr. Jon Davine
Psychiatry and Family Medicine
Hamilton, Ontario

Dr. Paul Hoaken
Psychiatry
Queen's University
Kingston, Ontario

Dr. Difat Jakubovicz
Family Medicine
Toronto, Ontario

Dr. Kola Oyewumi
Queen's University
Psychiatry
Kingston, Ontario

Dr. Tyrone Turner
Psychiatry
Toronto, Ontario

International

Dr. James A. Burns
Psychology
Lincoln, Nebraska

Dr. Davidson
Duke University

Dr. John H. Greist
U.W. Medical School
Psychiatry
Madison, Wisconsin

Dr. Richard G. Heimberg
Temple University,
Psychology
Philadelphia, PA

Dr. Debra A. Hope
Psychology
Lincoln, Nebraska

Dr. Matig R.
Mavissakalian
Case Western University
Psychiatry
Cleveland, Ohio

Dr. Mark Pollack
Psychiatry
Boston, Massachusetts

Pharmaceutical Manufacturers (9 companies)

Overview of Guideline Development Process

Development of Evidence Document
Systematic review of the anxiety literature[1]

↓

Multiple rounds of Delphi Review by the Panel

↓

Consensus Conference to review redrafted document

↓

External Validation/Consultation
Draft circulated to clinicians, manufacturers, and health professional associations across Canada and internationally for review and comment

↓

Comments from External Review presented in a blinded fashion to the Panel

↓

Document redrafted

Use of the Guidelines

These guidelines are intended to meet the needs of family physicians for concise, relevant advice when treating anxiety disorders. They can be used as a practical educational tool to assist primary care providers in providing care to patients with anxiety disorders. They have been developed by combining the best available research evidence with the expert clinical opinion of the panel members and clinicians from across the country using the process outlined above.

They are not being presented as a substitute for the knowledge of a physician or other knowledgeable provider, and they cannot take into account the unique needs of each patient or the variations in clinical resources available to a particular community or health care professional.

While every effort has been taken to assure the accuracy of the information, the Review Panel, publisher, printer and others contributing to the preparation of this document cannot accept liability for errors, omissions or any consequences arising from the use of the information. Since this document is not intended to replace other prescribing information, physicians are urged to consult manufacturer monographs and other available drug information literature before prescribing.

1. Cook DJ, Mulrow CD, Haynes RB. Systematic reviews: Synthesis of best evidence for clinical decisions. Annals of Internal Medicine. Systematic Review Series. 1997; 126(5): 376-380.
2. Canadian Task Force on the Periodic Health Examination: The periodic health examination. CMAJ 1979; 121: 1193-1254.

Table 1: Criteria for Level of Evidence Assignment[1]

Level	Description
I	**Good Research-Based Evidence** Well-conducted quantitative or qualitative research (e.g., randomized placebo-controlled trial) supported by substantial clinical experience.
II	**Fair Research-Based Evidence** Less well conducted quantitative or qualitative research (e.g., non-randomized studies) supported by substantial clinical experience.
III	**Expert Clinician Opinion** Minimal research-based evidence, but significant clinical experience.

Table 2: Criteria for Choice of Treatment Assignment

Treatment Choice	Description
FIRST LINE	Level I evidence and generally tolerable side effect/safety profile. It is generally recommended to begin therapy with a first line treatment. Second and third line treatments should be reserved for treatment resistant cases, intolerance or specific circumstances. Medications, for the most part, are listed in alphabetical order, while keeping agents of the same therapeutic class together.
SECOND LINE	Level II evidence or Level I evidence but less tolerable side effect/safety profile.
THIRD LINE	Level III evidence or Level I/II evidence and significantly less tolerable side effect/safety profile.
ADJUNCTIVE	Agents to consider using in addition to current where treatment outcomes have not been adequate following a trial with a first line agent on its own.

1. Cook DJ, Mulrow CD, Haynes RB. Systematic reviews: Synthesis of best evidence for clinical decisions. Annals of Internal Medicine. Systematic Review Services. 1997; 126(5): 376-380.
2. Modified from the Canadian Task Force on the Periodic Health Examination: The periodic health examination. CMAJ 1979; 121: 1193-1254.

Section II

Introduction

Anxiety Disorders in Primary Care

Anxiety disorders are characterized by symptoms of overriding nervousness, apprehension or tension serious enough to interfere with daily functioning. In the past few years the concept of anxiety as a symptom of a psychological disorder has undergone considerable change. Until recently anxiety symptoms have been thought to be either variations of a normal response to stress or an indication that the anxious person is suffering from unresolved conflicts. Anxiety can be considered a normal and natural, healthy response to life's challenges or threats, however, it needs to be recognized when it becomes pathological. Anxiety may be regarded as a problem needing treatment when it is of a different quality and of greater intensity and/or duration than normally expected within that family, society or culture, and leads to impairment in occupational, social or daily functioning.

Culturally, we are also seeing a change as the layperson begins to understand the various syndromes of anxiety that cause functional losses. Similar to the pathway depression has had to forge, we hope to see pathological anxiety move away from being perceived as a "weakness of character." Studies have repeatedly shown that there are significant quality of life gains to be made in treating anxiety disorders.

Factors that may predispose an individual to developing an anxiety disorder include environmental stressors, endocrine disturbances, use of certain substances or medications, and genetic predisposition. Most likely a combination of these factors may be responsible.

Anxiety disorders are diverse and not always easily classifiable. Therefore, recognizing pathological anxiety and selecting appropriate therapy can be challenging. Patients generally complain of unpleasant and unwarranted feelings of apprehension that are serious enough to disrupt normal daily activities. Sometimes anxiety is accompanied by physiologic symptoms (e.g., sweating, increased heart rate, shortness of breath), which usually remain consistent from one episode to the next. For most anxious patients their anxiety produces a degree of suffering that is underestimated by outside observers. They are often acutely aware that their symptoms are outside the normal experience, but due to attitudes or beliefs about mental health, choose to hide these reactions from others, especially caregivers and may be reluctant to seek professional help. For example, the average delay for the diagnosis of obsessive-compulsive disorder is between five and ten years.

Anxiety is conspicuously absent from various databases of systematic reviews such as the Cochrane Library and, as well, head-to-head trials of different medications are often lacking. As a result the treatment literature for many anxiety disorders is inconclusive with respect to what constitutes relative efficacy or the "best therapy". Studies do support the effectiveness of pharmacologic and psychological therapies for the treatment of many anxiety disorders encountered in clinical practice. The main drawback to psychological therapy is its limited availability, since few clinicians are trained in providing this type of treatment, particularly in rural areas. However self-administered psychological therapies are available through the use of books, audiocassettes and soon computer-based programs. Given the mounting evidence for Cognitive-Behavioural Therapy (CBT) it is to be hoped that this will become an educational priority in the future.

As most people have regular contact with primary health care services, patients with anxiety disorders are likely to see their family physician even though their psychological problem may not be the reason for the consultation. Therefore, the challenge to family physicians lies in being able to identify those with anxiety that require treatment and to select appropriate therapy.

Differentiating Among the Anxiety Disorders [1]

PHOBIC GROUP

Panic Disorder with or without Agoraphobia	• Sudden, recurrent episodes of intense anxiety or panic attacks that occur "out of the blue", with no situational trigger • Focus of anxiety is often expectation of having another attack • Wide range of physical symptoms occur • With or without agoraphobia, the fear of being in situations where a panic attack is likely to occur	**Page 23**
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TRAUMA AND STRESS RELATED

Post-Traumatic Stress Disorder	• Transient anxiety involving intense fear, helplessness or horror in response to a traumatic event (e.g., combat, abuse, natural disaster) • Symptoms: nightmares, flashbacks, intrusive memories, avoidance • Duration is more than 1 month • May experience panic attacks when exposed to trigger • **Acute Stress Disorder:** Symptoms develop within 4 weeks of event and last no longer than 1 month	**Page 32**

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Obsessive-Compulsive Disorder	• Presence of recurrent, unwanted thoughts, images or urges (**obsessions**) associated with compulsive, repetitive rituals (**compulsions**) in an attempt to reduce the related anxiety (e.g., fear of contamination causing repeated hand washing) • The anxiety is generally not about an everyday concern	**Page 35**

1. Note that there are three other anxiety disorders that are not addressed in this guideline: Anxiety Disorder Not Otherwise Specified, Anxiety Disorder due to a General Medical Condition, and Anxiety Disorder due to a Substance.

Assessment Summary

Clinical suspicion of anxiety?	• Anxiety/worry out of proportion to the problem • Phobic avoidance of feared situations • High utilization of medical services (e.g.., escalating self diagnosis, chronic dermatological problems, cancer-phobia, large medical chart) • High reactivity/side effect rate with medications • Functional losses, ranging from sudden loss (e.g., with onset of panic attacks) to chronic limitation (e.g., restricted ability for positive interaction with social phobia) • Associated symptoms: ➢ Irritability ➢ Sleep disturbance ➢ Appetite disturbance ➢ Difficulty concentrating ➢ Motor tension ➢ Autonomic hyperactivity ➢ Loss of energy ➢ Social withdrawal ➢ Obsessions, compulsions ➢ Chronic somatization **See Appendix A for "red flags" for detection of anxiety.**
Risk Factors?	• Family history of anxiety or depression • Past history of anxiety • Stressful life event • Increased burden of determinant of health (e.g., poverty, unemployment) • Isolated (poor social support) • Comorbidity with other psychiatric diagnosis • Gender [women are twice as likely to present with panic disorder, GAD, and some specific phobias (e.g., animal phobias but *not* height or needle phobias) than men].
Differential diagnoses?	Rule out or address other possible causes of anxiety or anxiety-like symptoms: • Post MI, angina or cardiac arrhythmias, hyperthyroidism, diabetes, asthma or chronic obstructive pulmonary disease, hypoglycemia, pheochromocytoma (extremely rare). • Somatoform disorders (e.g., hypochondriasis, body dysmorphic disorder), impulse control disorders (e.g., trichotillomania), depression • Psychotic disorder, some personality disorders, pervasive developmental disorder or eating disorder
Related to current medications?	Investigate whether anxiety symptoms related to use or abuse of: • Amphetamines, ephedrine, pseudoephedrine, aminophylline, theophylline, antihistamines, methylphenidate, thyroid preparations, over-the-counter drugs for colds/decongestants • Diet pills, appetite suppressants or wake up pills Rule out possible withdrawal symptoms from alcohol, benzodiazepines, anxiolytics, street drugs, narcotics

Assessment Summary (continued)

Potential substance abuse?	• Assess for substance abuse of alcohol, nicotine, caffeine (coffee, tea, cola drinks), cocaine, cannabis, amphetamines • Consider treating first, or concurrently with anxiety • Co-existence of substance abuse may seriously impair a patient's follow through with anti-anxiety therapy
Comorbid depression?	• Assess for depressive symptoms (high rates of coexistence with anxiety disorders 40-60%) • Associated with poorer recovery rates, greater psychosocial impairment, and higher relapse rates
Risk of suicide or self-harm?	• Anxiety disorders have a cumulative effect on risk of suicide when associated with other mental disorders (e.g., depression) • Deliberate self-harm (without intention of dying) often associated with anxiety as a means to cope with painful emotions and reduce tension • Consider involving mental health services
Additional assessment	• Root of the stress? (e.g., bereavement, job loss, divorce etc.) • Timing and nature of symptoms (seasonal, chronic, relation to life events) • Extent of disability and functional impairment (work, relationships) • Co-morbidity (e.g., depression)
Develop a Management Plan	

See Appendix B for Diagnostic Algorithm.

Treatment Summary

Goals of Treatment

Set realistic goals to be reached. For some anxiety disorders such as generalized anxiety disorder, panic disorder and social phobia, a goal of total absence of symptoms may be realistic. For obsessive-compulsive disorder and post-traumatic stress disorder, improvement to residual symptoms is more attainable.

STEP 1: PATIENT PSYCHOEDUCATION	
General information	Patients with any anxiety disorder benefit from education provided by the family physician. This includes: • Describing the nature of anxiety disorder, including physical symptoms, and confirming that it does exist. • Emphasizing the commonness of anxiety conditions • Informing that anxiety disorder can run in families. • Emphasizing that there is a good recovery rate. • Reviewing possible causes (e.g., stressful life event, isolation, another illness, addiction, medications). • Alerting that this disorder can lead to alcohol over-consumption. • Providing an overview of effective treatment options. • Setting expectations regarding drug and non-drug interventions (i.e., onset of benefit, side effects, chance for good response). • Directing to available reading (See Appendix E). • Providing hope to the patient. • Slow diaphragmatic breathing (See Appendix B).
Lifestyle advice and Non-drug strategies	• Decrease excessive use of caffeine (includes colas), alcohol, nicotine and chocolate. • Minimize use of sedatives or hypnotics. • Regular aerobic exercise (e.g., 20-40 minutes 3-5 times per week) • Manipulate diet and eat regularly spaced meals. • Alcohol or marijuana are commonly used to try to alleviate anxiety, however, they can precipitate panic and anxiety in the withdrawal phase. • Relaxation and breathing retraining techniques may be helpful. (See directions page 30)
Community resources	• If appropriate, and where available, involve a local mental health program or other support groups. • If appropriate, referral to other health care professionals, such as occupational therapists.
Supportive counselling	• Can be useful to address current life events and devise coping mechanisms by conveying encouragement and hope. • Helpful for chronic and life situation stress Note: Stress is defined as physiological arousal resulting from life problems the patient cannot adequately solve or deal with otherwise.

STEP 2: TREATMENT OPTIONS
1. Self Management / Treatment Includes provision of materials and appropriate sources for treatment manuals and information (See Appendix E: manuals, websites)
2. Pharmacotherapy
3. Therapist Assisted Cognitive-Behaviour Therapy (CBT)

There are 3 main treatment options: self-treatment, pharmacotherapy and therapist assisted cognitive-behavioural therapy, alone or in combination.

Treatment selection is dependent on numerous factors, some of which include: patient characteristics and preference, previous response to treatment, previous response of a family member, accessibility to each approach, short-term vs. long term goals, patterns of comorbidity, medical issues (e.g., pregnancy), sensitivity to side effects, skills of the clinician, relative costs and the availability of resources.

There is still much debate regarding the relative and combined efficacy of medications and CBT. As well, it is difficult to predict which will work best in different patients and to know the sequence in which to try different therapies. A general approach to the treatment of anxiety disorders is as follows:

1. Try a therapy

- Consider patient preference and motivation. If accessible and there are no patient compliance concerns try CBT first where possible. The family physician can play a key role in stimulating the patient's motivation to participate in CBT. One suggestion is to select an appropriate resource (e.g., workbook) and, if the patient is willing, have them review an appropriate chapter and discuss the assignment at the next visit. A Glossary of CBT terms is provided in Appendix B.
- Specific psychotherapy and pharmacotherapy recommendations are provided for each anxiety disorder.

2. Carry out a full course of treatment

3. Monitoring of progress

- Few standardized scales measuring the severity of anxiety symptoms have been validated, as well as many others that have not been validated in the primary care setting. One big problem is scale selection. Unlike depression, which is more or less a unitary construct, anxiety disorders consist of six very different problems and there is no measure that is appropriate for measuring all of the key features (e.g., physical manifestations, worry, panic attacks, obsessions, avoidance, etc.).

- A patient's progress can be monitored by having the patient document key symptoms (e.g., panic attacks), their frequency and duration, detailing the situation and triggers, and what they did to try to cope with the situation.

4. Evaluate the outcomes of treatment

- Consider using of the available scales or a self-report scale in a workbook.

5. Adjust the treatment if necessary

- Increase the current therapy (e.g., increase the intensity of CBT treatments or the dosage of the medication), add an adjunct medication or CBT, or change to a new treatment. Very little is known about sequencing of different therapies.

6. Duration of pharmacotherapeutic treatment

- The main goal in the acute phase is a reduction in or resolution of symptoms. This phase is usually of 12 weeks duration or more. In the next phase, the dose is optimized for maximum response to allow normal functioning and minimize side effects. While the optimal length of therapy is not known, a 12 month trial is not unreasonable.

Cognitive-Behavioural Therapy

Cognitive-Behavioural Therapy (CBT) is a type of psychotherapy that attempts to change the thoughts and behaviours that are fundamental to maintaining the anxiety disorder. Many forms of CBT exist. There is evidence that CBT is effective in the management of each of the anxiety disorders.

Generalized anxiety disorder, phobias, panic disorder, and posttraumatic stress disorder can be managed well with behaviour therapy. CBT can provide a very quick and effective therapy for treating specific phobias (i.e., a single 3-hour session).

Generally, the therapist assumes the role of a guide or coach for the patient, helping the individual understand the symptoms of anxiety and the current problems or demands facing him or her. The patient learns to identify the images that provoke anxiety or automatic thoughts, and methods for dealing with these thoughts and avoidance behaviours. Over time, as the patient masters various coping skills, (s)he gains confidence with new found competence in managing the anxiety and can work on addressing underlying problems. With behaviour therapy, behaviours change first and then changes in cognition and affect follow. With cognitive therapy, cognitions change first and then changes in affect and behavior follow. Cognitive therapy may be used to provide a rationale to patients for engaging in exposure therapy.

A glossary of cognitive-behavioural therapy terminology appears in Appendix B.

Patient factors that may favour CBT over pharmacotherapy:

- Avoidance behaviour and lifestyle problems
- Previous failure of pharmacotherapy
- Intact ability to concentrate
- Willingness to comply with self-help or homework assignments
- Capacity to consider and understand psychological factors
- Preference for CBT
- Previous success with CBT
- Access to CBT

Response to treatment

- CBT response may not be as fast as medication for some conditions, but it may have a longer lasting effect compared to medication, where there is a high rate of relapse after cessation of medication.

Consider referral for provision of cognitive-behavioural therapy.

- There may be limited access to qualified individuals. More advanced cognitive and behavioural therapies are provided by many clinical psychologists and some psychiatrists.
- These professionals should have: (a) evidence (such as tertiary qualification) of a theoretical understanding of personal and interpersonal behaviour and psychological dysfunction, (b) understanding, knowledge and skills in techniques for effecting change, (c) understanding of their own values, beliefs, emotions, relationships, and how these affect the process of therapy, (d) adherence to ethical standards (e.g., by membership of a professional association with ethical and disciplinary procedures), and (e) ongoing professional supervision to help maintain the quality of their work.

Pharmacotherapy

General Prescribing Tips

- *Appendix D* contains a summary of drugs used to treat anxiety and information on the use of benzodiazepines and the management of benzodiazepine withdrawal.

- ***Ensure that the patient understands the goals of treatment.***
  Set expectations regarding the role of drug intervention, target symptom(s), onset of benefit and onset of side effect(s), and chance for a good response.

- ***Start Low, Go Slow.***
  The approach to dosing is important in treating anxiety disorders, since patients are often sensitive to medication and very afraid of side effects. Antidepressants and anxiolytics must be started at low doses and gradually increased in order to maximize tolerability. Antidepressants may worsen or aggravate anxiety upon initiation due to their side effects; therefore, treatment must be initiated at low doses and consideration should be given to adding short-term benzodiazepine therapy given their faster onset of action to help the patient tolerate the antidepressant until the onset of its therapeutic effects. Dosages and length of treatment will vary with different disorders; consult appropriate sections in this guideline for individual disorders.

- ***Explain to patients they may feel worse before they feel better.***
  They may feel the negative consequences of drug treatment (e.g., side effects) without the benefit for a few weeks.
  Encourage them to contact you if they have any concerns; see them one week after starting a new medication for follow-up.

- ***Aim high enough.***
  Achieving an adequate dose is important to optimize therapeutic effects.

- ***Ensure an adequate length of trial.***
  The onset of effect is gradual with any medication chosen. It may be variable depending on the disorder being treated, the medication selected, as well as individual patient characteristics. However, in general, some therapeutic effect is seen within 6 weeks of treatment except in obsessive-compulsive disorder (OCD) and social phobia, in which 6 to 12 weeks of therapy may be required. Many referrals occur despite appropriate choice of treatment because of an inadequate trial period.

Section III

Anxiety Disorders and Therapies

Panic Disorder with or without Agoraphobia

In order to diagnose panic disorder, it may be necessary to perform a range of clinical tests, depending on the patient's age and physical health, since a wide range of physical symptoms may accompany attacks. It may be helpful to introduce Panic Disorder as a diagnostic possibility at the beginning of 'working up' the patient to rule out other physical causes. This allows them some time to contemplate this possibility and increased awareness that panic can be a very physical illness. A good diagnostic clue is that increased utilization of primary care services by panic patients is quite common. Refer to Appendix C for criteria for diagnosis.

Diagnostic Questions

1. Have you had any sudden episodes of intense anxiety, fear and discomfort, and physical symptoms? Can you describe what happens?
   Intensity usually peaks quickly and lasts about 20 minutes. Physical symptoms may include palpitations, sweating, trembling, dizziness, chest pain, chills, hot flashes and nausea.
2. Have some of the attacks occurred 'out of the blue'?
3. How often has this happened? How long do these spells generally last? Do they occur during the day or at night or both?
   Note that attacks can occur up to several times per day and can be nocturnal.
4. Do you feel anxious in certain situations?
5. Are you worried about having another panic attack?
6. Do the panic attacks occur in conjunction with a fear of being in a particular place or situation?
   Note that this can develop a few days or months after an attack.
7. Have the attacks caused you to restrict your daily activities in any way?

Treatment of Panic Disorder with or without Agoraphobia

The goal of treatment is to eliminate symptoms of the attacks, of anticipatory anxiety and of avoidance.

Psychological Therapies[1,2]	
FIRST LINE	**CBT (Cognitive Behavioural Therapy)** **Strategies may include:** • **Psychoeducation** • **Self-help manuals** • **Exposure to symptoms or situations** • **Cognitive restructuring** • **Breathing retraining** • **Continuous panic monitoring**

1. Note that intervention packages combining exposure exercises and cognitive restructuring techniques have become the psychosocial treatments of choice for panic and agoraphobia.
2. See Appendix B for Glossary of CBT Terms.

M121

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micromedia
a division of IHS Canada

20 Victoria Street
Toronto, Ontario M5C 2N8
Tel.: (416) 362-5211
Toll Free: 1-800-387-2689
Fax: (416) 362-6161
Email: info@micromedia.on.ca

Place in Therapy	Medication	Starting Dose	Usual Dosage*	Cost per day *
Panic Disorder with or without Agoraphobia				
FIRST LINE	CITALOPRAM [1] (Celexa)	10-15mg daily	20-30mg daily	$1.25-1.88
	FLUOXETINE (Prozac)	5-10mg daily	20-80mg daily	$1.01-4.04
	FLUVOXAMINE (Luvox)	25mg daily	50-300mg daily	$0.55-2.97
	PAROXETINE (Paxil)	10mg daily	40-60mg daily	$3.18-3.38
	SERTRALINE (Zoloft)	25-50mg daily	50-200mg daily	$1.60-3.50
	VENLAFAXINE (Effexor)	XR: 37.5mg daily; Regular: 9.375mg BID	75-150mg daily	$1.56-1.65
SECOND LINE	CLOMIPRAMINE (Anafranil)	50-75mg daily	75-200mg daily	$0.63-1.63
	DESIPRAMINE (Norpramin)	10-25mg daily	150-300mg daily	$1.27-2.53
	IMIPRAMINE (Tofranil)	10-25mg daily	150-300mg daily	$0.06-0.11
THIRD LINE	MOCLOBEMIDE (Manerix)	75-150mg BID	225-300mg BID	$1.22-2.28
	NEFAZODONE (Serzone)	25-50mg BID	150-300mg BID	$1.60-3.20
	PHENELZINE (Nardil)	7.5-15mg BID	15-30mg TID	$0.90-1.80
ADJUNCTIVE OR THIRD LINE	ALPRAZOLAM [2] (Xanax)	0.25-0.5mg TID	0.5-2mg TID	$0.28-1.66
	CLONAZEPAM [2] (Rivotril)	0.25-0.5mg daily	0.5-2mg BID	$0.23-0.40
	LORAZEPAM [2] (Ativan)	0.5-1mg BID	1-5mg TID	$0.09-0.39

1. Although Citalopram has only recently been introduced to the North American market there exists a strong European literature and clinical history.
2. There is evidence for the use of benzodiazepines and their role in therapy was a topic of some debate. While they do have a therapeutic role in a specific subset of patients, their usefulness is offset by a number of downsides (i.e., increased falls, MVAs, memory changes, withdrawal issues). BZDs may be useful as an adjunct to treatment with an SSRI or TCA, especially in the short time period before the SSRI/TCA takes effect. As an adjunct, BZDs should be used at low doses or p.r.n. and for short duration, since they are associated with risk of dependence and withdrawal syndromes. If being used as an only agent they should be used regularly. For more information see Appendix D.

4

Place in Therapy	Medication	Starting Dose	Usual Dosage+	Cost per day*
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Therapeutic Tips for Panic Disorder

Take symptoms seriously

Often people are afraid to tell their family physicians about panic and phobias because they fear this could jeopardize other complaints being taken seriously. The lifetime prevalence rate of panic disorder is approximately 3%.

Always include lifestyle advice and supportive counseling

Information on lifestyle, diet, symptoms, causes, and available treatments is helpful. Many find that reducing stimulants such as caffeine can significantly reduce the frequency of attacks; alcohol or marijuana use can precipitate panic and anxiety in the withdrawal phase as patients commonly use these drugs to try to alleviate their anxiety.

Make use of education tools

Self-help treatment as an adjunct can be beneficial and there are many self-help books, self-help exposure and cognitive therapy guides, videotapes and audiotapes available (See Appendix D).

Initial treatment of severe cases should combine medication and Cognitive-Behavioural Therapy

No consistent differences have been shown in the efficacies of CBT, medications, and their combination over the short term. While many trials do not look at long term outcomes, there is a growing literature that supports better long term outcomes with fewer relapses with CBT compared to medications (Barlow, 2000; Marks, 1993). Little is known about the best way to sequence different treatments. If agoraphobia is present it is more important to include exposure as part of the CBT regimen. Antidepressants may enhance the effectiveness of exposure therapy. Including spouses in CBT improves response.

Short Term Pain for Long Term Gain

Although patients suffering from panic disorder and agoraphobia may feel a short-term relief when they avoid a given situation, in the long term this will perpetrate their problem. A graded plan of exposure with support is often most helpful.

Start Low, Go Slow

Start at low dose with gradual upward titration of medication until complete symptom remission is achieved. The goal is consistent usage rather than rapid escalation. Patients with panic disorder may have phobic concerns about taking medications which may require special attention. Also patients often exhibit increased sensitivity to non-benzodiazepine medication. Many patients tolerate medication when started on a low dose or alternating day dosage schedule. Initiation of antidepressant therapy is often associated with a worsening of anxiety, particularly if the initial dose is too high. As well, the non-benzodiazepine medications often have up to a 4-6 week time lag before onset of effect.

Therapeutic Tips for Panic Disorder (continued)

Duration of Treatment

Patients usually show some improvement with CBT or medication within 6-8 weeks. The acute phase of treatment generally lasts about 12-16 weeks. After 12 weeks there should be a decrease in the frequency and intensity of panic attacks. The patient's anxiety about an attack should be minimal. It is recommended to maintain pharmacotherapy treatment for at least 1 year after response after which, if the patient maintains a full remission (zero panic attacks), the clinician can consider stopping therapy gradually over 2-6 months. Relapse is common following medication discontinuation and relapsing patients should begin taking medication again or be treated with CBT. Chronic therapy is required in 20-40% of patients. After the acute phase the frequency of visits for CBT decreases and CBT is discontinued within several months.

No response at 8-12 weeks

Re-evaluate the patient with regard to diagnosis or the need for a different treatment. Assess whether there is partial or no response to help guide whether dose needs to be increased versus medication substituted. Also ask the patient about compliance as some patients may decrease or stop their medication on their own for various reasons.

Social Phobia (also called Social Anxiety Disorder)

Social phobia is a type of anxiety that is often unrecognized and under-treated. The prevalence has been found to be as high as 13%, although there have been lower estimates as well. Social phobia occurs upon exposure to **social situations** and primarily impairs social, educational and occupational functioning. Success in these environments can significantly contribute to overall well-being, so while situations or events reported in isolation may seem benign, globally it can be quite limiting. Patients may also experience panic attacks when they are in social situations.

Generalized social phobia is characterized by anxiety in most social situations (e.g., initiating or maintaining conversations, dating, speaking to authority figures, attending parties). Often the anxiety in the generalized type is more severe and disabling. Generalized social phobia is the more common of the two subtypes, and is highly familial.

Discrete (performance phobia) differs from non-pathological performance anxiety because the latter peaks just after beginning the performance and subsequently abates. In addition, non-pathological performance anxiety undergoes habituation with repeated performances, whereas pathological anxiety continues with little, if any, habituation.

The symptoms can be grouped into 3 categories:

- **Cognitive:** fears of being embarrassed or humiliated, or negatively evaluated.
- **Physical:** blushing, muscle twitching, stammering, dry mouth, sweating, shaking, palpitations and diarrhea
- **Behavioural:** avoidance is the hallmark feature. Functional impairment is evident in occupational and educational functioning and interpersonal relationships.

Diagnostic Questions

1. Do you feel very nervous when you are with people? Do you worry what other people think of you? Do you feel that this fear is unreasonable?
2. Do you feel anxious in certain situations? Is the anxiety related specifically to social situations or being in a place where you might be evaluated by other people?
3. Do you find that you're afraid of being the focus of attention?
4. Do you find that you avoid social situations?
5. Does this fear affect your work? Your relationships with others or your social life?

Treatment of Social Phobia

Psychological Therapies [1,2]
FIRST LINE CBT (Cognitive Behavioural Therapy) **Strategies may include:** • **Psychoeducation** • **Self-help manuals** • **Cognitive-Behavioural Therapy (CBT)** [1] • **Exposure to feared situations** • **Role playing and social skills training**

1.CBT is an effective treatment for social phobia. It is at least as effective as medications in the short-term and may be more effective in the long-term. Intervention packages combining cognitive restructuring techniques and exposure exercises have become the psychosocial treatments of choice.
2. See Appendix B for Glossary of CBT Terms

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Fax: (416) 362-6161
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Place in Therapy	Medication	Starting Dose	Usual Dosage+	Cost per Day*
Social Phobia – Generalized Type				
FIRST LINE	**FLUVOXAMINE (Luvox)**	**50-100mg daily**	**100-300mg daily**	$0.99-2.97
	PAROXETINE (Paxil)	**10-20mg daily**	**20-50mg daily**	$1.59-3.98
	SERTRALINE (Zoloft)	**25-50mg daily**	**50-100mg daily**	$1.60-1.75
	MOCLOBEMIDE[1] (Manerix)	**75-150mg BID**	**225-300mg BID**	$1.22-2.28
SECOND LINE	**CITALOPRAM[2] (Celexa)**	**10-15mg daily**	**20-30mg daily**	$1.25-1.88
	FLUOXETINE (Prozac)	**5-20mg daily**	**20-40mg daily**	$1.01-2.02
	VENLAFAXINE (Effexor)	**XR: 37.5mg daily; Regular: 18.75mg BID**	**75 mg-225mg daily**	$1.56-3.21
ADJUNCTIVE OR SECOND LINE	**ALPRAZOLAM[3] (Xanax)**	**0.25-1mg TID**	**0.25-3mg BID**	$0.23-1.66
	CLONAZEPAM[3] (Rivotril)	**0.5mg BID-TID**	**0.5-2mg BID**	$0.24-0.40
THIRD LINE	**PHENELZINE (Nardil)**	**7.5-15mg BID**	**15-37.5mg BID**	$0.60-1.50
	GABAPENTIN		**600-3600mg**	

1. While moclobemide has positive RCT data, 4 trials failed to differentiate from placebo due to high placebo response.
2. Although Citalopram has only recently been introduced to the North American market there exists a strong European literature and clinical history and several North American trials are currently on-going.
3. There is evidence for the use of benzodiazepines and their role in therapy was a topic of some debate. While they do have a therapeutic role in a specific subset of patients, their usefulness is offset by a number of downsides (i.e., increased falls, MVAs, memory changes, withdrawal issues). BZDs may be useful as an adjunct to treatment with an SSRI or TCA, especially in the short time period before the SSRI/TCA takes effect. As an adjunct, BZDs should be used at low doses or p.r.n. and for short duration. If being used alone they should be used regularly. For more information see Appendix D.

Social Phobia – Discrete (performance phobia)[1,2]

ALTERNATIVES	**ALPRAZOLAM (Xanax)**	**0.25mg p.r.n.**	
	LORAZEPAM (Ativan)	**0.5mg p.r.n.**	
	PROPRANOLOL[3] (Inderal)	**10 –20mg p.r.n.**	* **Cardiovascular medication**

1. Examples: eating in front of others, using public lavatories, performing, speaking in front of others.
2. Recommended behavioural interventions: exposure, role plays. Toastmasters (1-800-993-7732; www.toastmasters.org) can be helpful for public speaking anxiety.
3. Non-selective beta-blockers, like propranolol, are anecdotally effective in low doses for treating performance anxiety (stage-fright), however, they performed poorly in controlled trials and there is no evidence to support their usefulness in generalized social phobia. A test dose(s) prior to first use is recommended in order to prevent inducing hypotension at the time of first performance.

Place in Therapy	Medication	Starting Dose	Usual Dosage+	Cost per Day*
Social Phobia – Generalized Type				
FIRST LINE	**FLUVOXAMINE (Luvox)**	**50-100mg daily**	**100-300mg daily**	**$0.99-2.97**
	PAROXETINE (Paxil)	**10-20mg daily**	**20-50mg daily**	**$1.59-3.98**
	SERTRALINE (Zoloft)	**25-50mg daily**	**50-100mg daily**	**$1.60-1.75**
	MOCLOBEMIDE[1] (Manerix)	**75-150mg BID**	**225-300mg BID**	**$1.22-2.28**
SECOND LINE	**CITALOPRAM[2] (Celexa)**	**10-15mg daily**	**20-30mg daily**	**$1.25-1.88**
	FLUOXETINE (Prozac)	**5-20mg daily**	**20-40mg daily**	**$1.01-2.02**
	VENLAFAXINE (Effexor)	**XR: 37.5mg daily; Regular: 18.75mg BID**	**75 mg-225mg daily**	**$1.56-3.21**
ADJUNCTIVE OR SECOND LINE	**ALPRAZOLAM[3] (Xanax)**	**0.25-1mg TID**	**0.25-3mg BID**	**$0.23-1.66**
	CLONAZEPAM[3] (Rivotril)	**0.5mg BID-TID**	**0.5-2mg BID**	**$0.24-0.40**
THIRD LINE	**PHENELZINE (Nardil)**	**7.5-15mg BID**	**15-37.5mg BID**	**$0.60-1.50**
	GABAPENTIN		**600-3600mg**	

1. While moclobemide has positive RCT data, 4 trials failed to differentiate from placebo due to high placebo response.
2. Although Citalopram has only recently been introduced to the North American market there exists a strong European literature and clinical history and several North American trials are currently on-going.
3. There is evidence for the use of benzodiazepines and their role in therapy was a topic of some debate. While they do have a therapeutic role in a specific subset of patients, their usefulness is offset by a number of downsides (i.e., increased falls, MVAs, memory changes, withdrawal issues). BZDs may be useful as an adjunct to treatment with an SSRI or TCA, especially in the short time period before the SSRI/TCA takes effect. As an adjunct, BZDs should be used at low doses or p.r.n. and for short duration. If being used alone they should be used regularly. For more information see Appendix D.

Social Phobia – Discrete (performance phobia)[1,2]				
ALTERNATIVES	**ALPRAZOLAM (Xanax)**	**0.25mg p.r.n.**		
	LORAZEPAM (Ativan)	**0.5mg p.r.n.**		
	PROPRANOLOL[3] (Inderal)	**10 –20mg p.r.n.**		* **Cardiovascular medication**

1. Examples: eating in front of others, using public lavatories, performing, speaking in front of others.
2. Recommended behavioural interventions: exposure, role plays. Toastmasters (1-800-993-7732; www.toastmasters.org) can be helpful for public speaking anxiety.
3. Non-selective beta-blockers, like propranolol, are anecdotally effective in low doses for treating performance anxiety (stage-fright), however, they performed poorly in controlled trials and there is no evidence to support their usefulness in generalized social phobia. A test dose(s) prior to first use is recommended in order to prevent inducing hypotension at the time of first performance.

Specific Phobias (formerly called Simple Phobias)

Specific phobias are very prevalent and can affect daily functioning. Approximately 11% of the population has a specific phobia that interferes with their day-to-day activities. Generally, the person realizes that their fears are excessive, and may experience panic symptoms upon exposure to or in anticipation of exposure to the feared object or situation.

Diagnostic Questions

1. Do you fear specific situations or objects?
   For example: animals, medical procedures, heights.
2. Do you feel that this fear is excessive?
3. Do you find that you avoid places or situations where you might come into contact with this object or situation?
4. Does this fear affect your life?

Treatment of Specific Phobias

Psychological Therapies[1]	
FIRST LINE	• **In vivo exposure to feared stimuli**[2] **(with psychoeducation)**
SECOND LINE	• **Imaginal exposure**[2] **(if live exposure is not possible)** • **Cognitive restructuring**

1. See Appendix B for Glossary of CBT Terms
2. In vivo exposure therapy involves confronting the feared situations until the fear has decreased. It is done in a controlled manner in vivo or in imagination. Several of the large airlines have programs for people with a phobia of flying.

Medication
There is very little information available about the efficacy of medications. Anecdotal evidence suggests that a short course of a low dose benzodiazepine or anxiolytic (i.e., 0.125mg of clonazepam), which the patient can discontinue him or herself may be useful.

Therapeutic Tips for Specific Phobias

Take phobias seriously
Often people do not tell their family physicians about phobias because they feel embarrassed or ashamed about them, don't believe anything can be done or fear that other complaints may not be taken seriously.

Pattern of avoidance
People with certain phobias related to health care (e.g., blood, injections, surgery) may avoid going to see doctors.

Generalized Anxiety Disorder (GAD)

GAD is the most misdiagnosed of all anxiety disorders. It is a chronic disturbance characterized by excessive worry and apprehension where patients tend to focus on "what if" scenarios. A key issue is whether the patient's worry is unreasonable given their life situation.

It is not uncommon that patients experience GAD symptoms exclusively in depression. For a diagnosis of GAD, the person has to have experienced the worry at a separate time to depression. Increased utilization of primary care services is common.

Estimates of lifetime prevalence range from 4-6.6% with a 2:1 female: male ratio. Compared to other anxiety disorders GAD often has an early age of onset, however, patients actually present later in life.

Diagnostic Questions

1. On most days, do you find that you seem to be worrying about everyday things more than you think you should? (i.e., health, money, family)
2. Do other people think of you as being a 'worrier'? Are you described as a 'worry wart'?
3. Is the worry itself causing problems for you? Do you find it difficult to control?
4. How long have you found worrying to be a problem? Has it been longer than 6 months? *('As long as I can remember' is a typical response)*
5. During these periods of worry do you:
   Feel tense (restless, keyed up or on edge)
   Feel tired (weak or exhausted easily)? Have difficulty sleeping?
   Have difficulty concentrating or find your mind going blank?
   Feel irritable?
   Have muscle tension?
6. What ways do you try and cope with the worry? Is there anything that seems to help?
   (Note that alcohol is the oldest anxiolytic treatment.)
7. (If depression is also present) Do you have periods of excessive worry even during times when you are not feeling depressed?

Treatment of GAD

Psychological Therapies[1,2]	
FIRST LINE	**CBT (Cognitive Behavioural Therapy)** **Strategies may include:** • **Relaxation Training** • **Cognitive-Behavioural Therapy (CBT)** • **Psychoeducation**[3] • **Self-management**[3] • **Problem-Solving Training**[3]

1. See Appendix B for Glossary of CBT Terms
2. Psychological treatments with or without medication are recommended. With mild symptoms associated with psychosocial stressors, non-medication treatment may be satisfactory.
3. Although psychoeducation, problem-solving training, and supportive psychotherapy may be components of treatment, the only empirically supported psychological treatments are relaxation training, cognitive therapy, and their combination.

Place in Therapy	Medication	Starting Dose	Usual Dosage+	Cost per day *
Generalized Anxiety Disorder (GAD)[1]				
FIRST LINE	BUSPIRONE[2] (Buspar)	5mg TID	5-20mg TID	$1.45-5.82
	FLUVOXAMINE (Luvox)	50-100mg daily	100-300mg daily	$0.99-2.97
	PAROXETINE (Paxil)	10-20mg daily	20-60mg daily	$1.59-3.38
	VENLAFAXINE (Effexor)	XR: 37.5-75mg daily; Regular: 18.75-37.5mg BID	75-225mg daily	$1.56-3.21
SECOND LINE	CLOMIPRAMINE (Anafranil)	25mg daily	100-300mg daily	$0.82-2.45
	IMIPRAMINE (Tofranil)	50-75mg daily	100-250mg daily	$0.04-0.09
ADJUNCTIVE OR THIRD LINE	ALPRAZOLAM[3] (Xanax)	0.25-0.5mg BID-TID	0.25-1mg BID-TID	$0.15-0.55
	BROMAZEPAM[3] (Lectopam)	3mg BID – 6mg TID	3mg BID – 9mg TID	$0.18-0.65
	CLONAZEPAM[3] (Rivotril)	0.5mg BID-TID	0.5-2mg BID	$0.23-0.40
	DIAZEPAM[3] (Valium)	2-5mg BID-TID	2.5-10mg BID -QID	$0.01-0.03
	OXAZEPAM[3] (Serax)	10-15mg TID-QID	15mg BID-30mg QID	$0.02-0.05

1. Factors in favour of medication include chronicity, absence of substance abuse, potential for compliance, lack of clearly identified psychosocial stressors.
2. Although buspirone has RCT level evidence, the overall impression is that it is a weaker anxiolytic and not useful if comorbid panic is present.
3. There is evidence for the use of benzodiazepines and their role in therapy was a topic of some debate. While they do have a therapeutic role in a specific subset of patients, their usefulness is offset by a number of downsides (i.e., increased falls, MVAs, memory changes, withdrawal issues). BDZs work most quickly (1 to 2 weeks) but may cause rebound anxiety upon taper or withdrawal. While they may be useful as an adjunct to treatment with an SSRI/ TCA in the short time period before the SSRI/TCA takes effect, this role is limited in GAD which is generally less severe than other anxiety disorders. As an adjunct, BZDs should be used at the lowest dose that alleviates anxiety or p.r.n. and for short duration. If being used alone they should be used regularly. BDZs may be appropriate longterm if a patient does not respond to other therapy. For more information see Appendix D.

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SECOND LINE	CLOMIPRAMINE (Anafranil)	25mg daily	100-300mg daily	$0.82-2.45
	IMIPRAMINE (Tofranil)	50-75mg daily	100-250mg daily	$0.04-0.09
ADJUNCTIVE OR THIRD LINE	ALPRAZOLAM[3] (Xanax)	0.25-0.5mg BID-TID	0.25-1mg BID-TID	$0.15-0.55
	BROMAZEPAM[3] (Lectopam)	3mg BID – 6mg TID	3mg BID – 9mg TID	$0.18-0.65
	CLONAZEPAM[3] (Rivotril)	0.5mg BID-TID	0.5-2mg BID	$0.23-0.40
	DIAZEPAM[3] (Valium)	2-5mg BID-TID	2.5-10mg BID -QID	$0.01-0.03
	OXAZEPAM[3] (Serax)	10-15mg TID-QID	15mg BID-30mg QID	$0.02-0.05

1. Factors in favour of medication include chronicity, absence of substance abuse, potential for compliance, lack of clearly identified psychosocial stressors.
2. Although buspirone has RCT level evidence, the overall impression is that it is a weaker anxiolytic and not useful if comorbid panic is present.
3. There is evidence for the use of benzodiazepines and their role in therapy was a topic of some debate. While they do have a therapeutic role in a specific subset of patients, their usefulness is offset by a number of downsides (i.e., increased falls, MVAs, memory changes, withdrawal issues). BDZs work most quickly (1 to 2 weeks) but may cause rebound anxiety upon taper or withdrawal. While they may be useful as an adjunct to treatment with an SSRI/ TCA in the short time period before the SSRI/TCA takes effect, this role is limited in GAD which is generally less severe than other anxiety disorders. As an adjunct, BZDs should be used at the lowest dose that alleviates anxiety or p.r.n. and for short duration. If being used alone they should be used regularly. BDZs may be appropriate longterm if a patient does not respond to other therapy. For more information see Appendix D.

Post-Traumatic Stress Disorder

Exposure to an extraordinary trauma is a requirement for PTSD. Those more likely to develop PTSD are those with a previous history of psychiatric disorders and other risk factors, such as previous exposure to a traumatic event. PTSD is very complex disorder that often presents with comorbid complications, such as substance abuse, other anxiety disorders and depression.

Acute Stress Disorder

Potential sufferers of PTSD may first suffer from Acute Stress Disorder (ASD). The symptoms of ASD are similar to PTSD, but the duration of the symptoms is shorter. ASD symptoms occur within 4 weeks of the traumatic event, and lasts a minimum of 2 days and maximum of 1 month, whereas PTSD is longer than 1 month. Early treatment of ASD can help to prevent the development of PTSD.

Diagnostic Questions

1. Is the anxiety related to a severe traumatic event?
   For example: combat, sexual abuse, natural disaster, serious accident, refugee, witness to a traumatic event.
2. Have you experienced the anxiety around this event for longer than 1 month?
3. Have you been troubled by 're-experiencing' of the events?
   For example: intrusive distressing recollections, flashbacks, nightmares, sense of reliving the event.
4. Has the event caused you to avoid activities, thoughts or places related to the trauma?
5. Do you find you're feeling more detached from others than previously?
6. Do you have any difficulty sleeping? Difficulty concentrating? Unusual irritability?
7. Are there any triggers that bring on symptoms?
8. Do you get panic attacks?

Treatment for PTSD

PTSD is often chronic and significant improvement or resolution in the short term may not be realistic.

Cognitive therapy

Psychoeducation and supportive counselling by the family practitioner should begin immediately. Overall, studies of CBT have yielded the most promising findings. If symptoms have lasted for at least 1 month without significant improvement, offer or refer for psychological treatment. Support groups may be beneficial.

Medication

Consider prescribing medication if symptoms are significant, daily functioning is severely disrupted, the patient has severe insomnia, a co-morbid psychiatric condition is present, or if the patient is still having significant symptoms following psychotherapy.

Psychological Therapies[1]

FIRST LINE CBT (Cognitive Behavioural Therapy)

Strategies may include:

- **Psychoeducation**[2]
- **Self-help/ Management**
- **Cognitive Therapy**[3]
- **Stress inoculation training**[4]
- **Imaginal exposure**[5]
- **Exposure in vivo to safe triggers of generalized avoidance**
- **Supportive counselling**[6]

SECOND LINE

- **EMDR (Eye-Movement Desensitization and Reprocessing)**[7]

1. See Appendix B for Glossary of CBT Terms
2. If possible, therapy should begin ***immediately*** following the trauma and should include the following:
   - Help the patient understand that it is normal to be upset and have distressing symptoms shortly after a trauma.
   - Encourage them to talk with family and friends about the trauma and associated feelings.
   - Educate the family about the importance of listening, being tolerant of the person's emotional reactions, and accepting the need for repeated retelling of the event.
   - Provide emotional support and relieve irrational guilt.
   - Refer to peer support group or trauma counselling.
   - Consider short-term sleep medication for insomnia.
3. Cognitive therapy: correct irrational beliefs, especially unrealistic guilt about the trauma.
4. Stress inoculation training: relaxation training, breathing retraining, positive thinking/self-talk, and assertiveness training.
5. In cases of rape victims, prolonged imaginal exposure may be preferable to stress inoculation training.
6. Supportive therapy is appropriate for the grief reaction. Group therapy may be helpful.
7. EMDR has been shown to be useful, but the effective element is probably imaginal exposure and not the eye movements.

M121

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20 Victoria Street
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Place in Therapy	Medication	Starting Dose	Usual Dosage*	Cost per day*
Post-Traumatic Stress Disorder [1,2]				
FIRST LINE	FLUOXETINE (Prozac)	5-20mg daily	20-40mg daily	$1.01-2.02
	SERTRALINE (Zoloft)	25-50mg daily	50-150mg daily	$1.60-3.35
	AMITRIPTYLINE (Elavil)	50-75mg daily	100-250mg daily	$0.03-0.08
	IMIPRAMINE (Tofranil)	50-75mg daily	100-250mg daily	$0.04-0.09
SECOND LINE	FLUVOXAMINE (Luvox)	50-100mg daily	100-300mg daily	$0.99-2.97
	PAROXETINE (Paxil)	10-20mg daily	20-60mg daily	$1.59-3.38
	VENLAFAXINE (Effexor)	XR: 37.5-75mg daily; Regular: 18.75-37.5mg BID	75-225mg daily	$1.56-3.21
	NEFAZODONE (Serzone)	100mg daily	300-500mg daily	$1.60-2.33
	PHENELZINE (Nardil)	7.5-15mg BID	15-37.5mg BID	$0.60-1.50
ADJUNCTIVE Anti-anxiety	ALPRAZOLAM (Xanax)	0.25-0.5mg BID-TID	0.25-1mg BID-TID	$0.15-0.55
	BUSPIRONE (Buspar)	5mg TID	5-20mg TID	$1.45-5.82
	CLONAZEPAM (Rivotril)	0.5mg BID-TID	0.5-2mg BID	$0.23-0.40
Mood Stabilizers	DIVALPROEX (Epival)	500mg daily	500-1500mg daily	$0.55-1.65

1. Less controlled research with pharmacologic agents has been conducted, and studies have yielded conflicting results. If symptoms have lasted for at least 1 month without significant improvement consider prescribing medication if symptoms are severe, daily functioning is disrupted, or if there is severe insomnia, comorbid depression, anxiety or suicidal tendencies or if patient has already been receiving psychotherapy and is still having significant symptoms.
2. Start with an SSRI for at least an 8 week treatment trial. Evaluate response every 1-2 weeks and increase dose as needed. After 8 weeks of SSRI trial:
   - If no response, switch to nefazodone or venlafaxine
   - If partial response, add a mood stabilizer such as divalproex.

If patient has other significant problems, consider:
   - For severe insomnia, short-term treatment with trazodone
   - For significant anxiety, short-term treatment with a benzodiazepine or longer term treatment with buspirone
   - For comorbid bipolar disorder, severe irritability, or aggressive behaviour, add a mood stabilizer.

Place in Therapy	Medication	Starting Dose	Usual Dosage[+]	Cost per day[*]
Post-Traumatic Stress Disorder [1,2]				
FIRST LINE	FLUOXETINE (Prozac)	5-20mg daily	20-40mg daily	$1.01-2.02
	SERTRALINE (Zoloft)	25-50mg daily	50-150mg daily	$1.60-3.35
	AMITRIPTYLINE (Elavil)	50-75mg daily	100-250mg daily	$0.03-0.08
	IMIPRAMINE (Tofranil)	50-75mg daily	100-250mg daily	$0.04-0.09
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ADJUNCTIVE Anti-anxiety	ALPRAZOLAM (Xanax)	0.25-0.5mg BID-TID	0.25-1mg BID-TID	$0.15-0.55
	BUSPIRONE (Buspar)	5mg TID	5-20mg TID	$1.45-5.82
	CLONAZEPAM (Rivotril)	0.5mg BID-TID	0.5-2mg BID	$0.23-0.40
Mood Stabilizers	DIVALPROEX (Epival)	500mg daily	500-1500mg daily	$0.55-1.65

1. Less controlled research with pharmacologic agents has been conducted, and studies have yielded conflicting results. If symptoms have lasted for at least 1 month without significant improvement consider prescribing medication if symptoms are severe, daily functioning is disrupted, or if there is severe insomnia, comorbid depression, anxiety or suicidal tendencies or if patient has already been receiving psychotherapy and is still having significant symptoms.
2. Start with an SSRI for at least an 8 week treatment trial. Evaluate response every 1-2 weeks and increase dose as needed. After 8 weeks of SSRI trial:
   - If no response, switch to nefazodone or venlafaxine
   - If partial response, add a mood stabilizer such as divalproex.

If patient has other significant problems, consider:
   - For severe insomnia, short-term treatment with trazodone
   - For significant anxiety, short-term treatment with a benzodiazepine or longer term treatment with buspirone
   - For comorbid bipolar disorder, severe irritability, or aggressive behaviour, add a mood stabilizer.

Obsessive-Compulsive Disorder

Obsessive-Compulsive Disorder is a *recurrent and persistent illness*. The lifetime prevalence rate of OCD in adults is approximately 2.5%. There is common co-morbidity with social phobia and depression. Note that patients who exhibit only tics or skin-picking problems do not generally have OCD.

Diagnostic Questions

1. Are you experiencing recurrent, unwanted thoughts, images or urges?
2. Are these thoughts causing you to do anything repeatedly and compulsively? (e.g., hand washing, checking the doors, locks, stove.)
3. Do these thoughts keep coming back into your mind even when you try to ignore or get rid of them?
4. Do you think that these obsessive thoughts or repetitive behaviours are excessive or unreasonable? (If no, patient may be classified as having OCD *with poor insight*.)
5. Do these thoughts or behaviours significantly interfere with your normal routine, occupational functioning, usual social activities, or relationships? Do they take more than one hour a day?

Treatment

Psychotherapy: No consistent differences have been found in effectiveness of cognitive-behavioural therapy, medications and their combination. Behaviour therapy using exposure-response prevention is the treatment of choice for limiting the amount of dysfunction resulting from the obsessions/compulsions.

Medication: It is important to optimize the first line medications before moving to second line. If the patient is a non- or partial responder, consider trying three different - SRI agents before moving to a second line strategy such as addition of an adjunctive medication. Adequate treatment trial is 12 weeks at an optimal dosage. Dosages tend to be higher than those used for the treatment of depression. As many as 40-60% of OCD patients do not respond to an adequate trial of SSRIs and most RCTs have shown only a 25% reduction in symptom severity in responders.

Assessment: behavioural assessment, monitoring diaries and self-report questionnaires

Psychological Therapies [1]	
FIRST LINE	**CBT (Cognitive Behavioural Therapy)** **Strategies may include:** • **Exposure and response prevention** [2]
ALTERNATIVE	• **Cognitive restructuring** • **Behavioural family therapy**

1. See Appendix B for Glossary of CBT Terms

2. Exposure-response prevention (ERP) has shown comparable treatment gains as clomipramine with lower relapse rates after treatment cessation. However, even treatment responders fail to achieve complete amelioration of symptoms.

Place in Therapy	Medication	Starting Dose	Usual Dosage[+]	Cost per day *
Obsessive-Compulsive Disorder				
FIRST LINE [1]	**CLOMIPRAMINE (Anafranil)**	**25mg daily**	**100-300mg daily**	$0.82-2.45
	FLUOXETINE (Prozac)	**20mg daily**	**20-80mg daily**	$1.01-4.04
	FLUVOXAMINE (Luvox)	**50mg daily**	**100-300mg daily**	$0.99-2.97
	PAROXETINE (Paxil)	**10-20mg daily**	**40-60mg daily**	$3.18-3.38
	SERTRALINE (Zoloft)	**25-50mg daily**	**50-200mg daily**	$1.60-3.50
	CITALOPRAM [2] **(Celexa)**	**20mg daily**	**20-60mg daily**	$1.25-2.50
SECOND LINE	**TRAZODONE (Desyrel)**	**25-50mg BID**	**100-200mg BID**	$0.79-1.58
	VENLAFAXINE (Effexor)	**XR: 37.5-75mg daily; Regular: 18.75-37.5mg BID**	**150-375mg daily (divided TID)**	$1.65-3.30
	NEFAZODONE (SERZONE)	**50-100 mg BID**	**150-200 mg BID**	$1.60-1.86
ADD ADJUNCTIVE THERAPY FOR NON OR PARTIAL RESPONDERS [3, 4]				
	HALOPERIDOL [3] **(Haldol)**	**0.5mg daily**	**2-4mg daily**	$0.11-0.22
	PIMOZIDE [3,5] **(Orap)**	**0.5-1mg daily**	**2-4mg daily**	$0.92-1.77
	RISPERIDONE [3] **(risperdal)**	**0.5mg daily**	**2-4mg daily**	$1.92-3.84
SECOND LINE ADJUNCTIVE THERAPY FOR NON OR PARTIAL RESPONDERS ***(Only for refractory, chronic patients)***				
	L-TRYPTOPHAN [4]	**0.5g daily**	**2-4g daily (max: 6g)**	
	LITHIUM [3,4]		**300mg BID-TID**	$0.13-20
	PINDOLOL (Visken)	**5 mg BID**	**10-20 mg BID**	$0.79-1.58
	GABAPENTIN (Neurontin)	**300-400 mg daily**	**300mg BID to 800 mg TID**	$1.95-6.96

1. In a non or partial responder consider trying 3 different SSRIs before adding an adjunctive agent or moving to a second line strategy. Adequate treatment trial is 12 weeks. Dosages tend to be higher than those used for the treatment of depression.
2. Only limited evidence is available for the use of citalopram in OCD.
3. Augmentation considerations: haldol or pimozide where there is poor patient insight regarding the condition; risperidone for generalized tic disorder; lithium for co-morbid depression.
4. Potential drug interactions should be considered before initiating adjunctive therapy, and patients monitored accordingly.
5. Available data suggest that pimozide is only useful when added to a 1st line agent.

Place in Therapy	Medication	Starting Dose	Usual Dosage[+]	Cost per day *
Obsessive-Compulsive Disorder				
FIRST LINE [1]	CLOMIPRAMINE (Anafranil)	25mg daily	100-300mg daily	$0.82-2.45
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4. Potential drug interactions should be considered before initiating adjunctive therapy, and patients monitored accordingly.
5. Available data suggest that pimozide is only useful when added to a 1st line agent.

Appendices

Appendix A

*RED FLAGS for Detection of Anxiety Disorders in Primary Care**

Symptom	Screening Questions
Anxiety/worry	Have you felt more worried than usual? Do you experience episodes of intense worry? Do these occur 'out of the blue'? Does the worry have a particular focus (e.g., finances, health, work- related, social performance, relationship)? Do you feel that your level of anxiety is excessive? Do you feel anxious in certain situations? Do you avoid being with people? Do you avoid being away from a place of safety?
Phobias	Do you fear social or performance situations? Do you avoid situations? Are there any specific things that you fear or avoid? Do you feel the fear is excessive?
Traumatized	Have you ever seen or had something happen to you that made you feel frightened or helpless? Do you have recurrent upsetting memories or images of this event? Do you avoid situations that may trigger memories?
Irritability	Have you or your family noticed that you have been more irritable lately?
Sleep disturbance	Have you had difficulty falling asleep or staying asleep? Do you find that you're easily fatigued?
Appetite disturbance	Have you lost your appetite?
Difficulty concentrating	Does your thinking seem slower or more confused than usual? Are you making more mistakes? Do you find your mind 'going blank'?
Motor tension	Have you felt agitated or on edge? Do you feel like you have to keep talking or moving all the time? Any tremor or muscle aches? (can also be observed)
Autonomic hyperactivity	Have you had any trouble with dizzy spells? Hot flashes or chills? Nausea or diarrhea?
Loss of energy	Have you been feeling tired or experiencing low energy?
Social withdrawal	Do you still participate in your usual activities or hobbies? Have you been less interested in interacting with others (family, co-workers)?
Obsessions	Any repetitive intrusive thoughts that bother or frighten you?
Compulsions	Anything you do repetitively? (Such as repeatedly checking door locks or the stove or washing hands?)
Dermatological Problems	Any skin problems (rashes, dermatitis, etc) for a prolonged period of time?
Chronic somatization	Repeated non response to treatment, pattern of recurrent investigations for a number of complaints where nothing comes up
Large medical chart	Tend to be chronic, frequent users of medical system

* Observed and reported behaviour should be incorporated into the evaluation.

Appendix A

*RED FLAGS for Detection of Anxiety Disorders in Primary Care**

Symptom	Screening Questions
Anxiety/worry	Have you felt more worried than usual? Do you experience episodes of intense worry? Do these occur 'out of the blue'? Does the worry have a particular focus (e.g., finances, health, work- related, social performance, relationship)? Do you feel that your level of anxiety is excessive? Do you feel anxious in certain situations? Do you avoid being with people? Do you avoid being away from a place of safety?
Phobias	Do you fear social or performance situations? Do you avoid situations? Are there any specific things that you fear or avoid? Do you feel the fear is excessive?
Traumatized	Have you ever seen or had something happen to you that made you feel frightened or helpless? Do you have recurrent upsetting memories or images of this event? Do you avoid situations that may trigger memories?
Irritability	Have you or your family noticed that you have been more irritable lately?
Sleep disturbance	Have you had difficulty falling asleep or staying asleep? Do you find that you're easily fatigued?
Appetite disturbance	Have you lost your appetite?
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Motor tension	Have you felt agitated or on edge? Do you feel like you have to keep talking or moving all the time? Any tremor or muscle aches? (can also be observed)
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Loss of energy	Have you been feeling tired or experiencing low energy?
Social withdrawal	Do you still participate in your usual activities or hobbies? Have you been less interested in interacting with others (family, co-workers)?
Obsessions	Any repetitive intrusive thoughts that bother or frighten you?
Compulsions	Anything you do repetitively? (Such as repeatedly checking door locks or the stove or washing hands?)
Dermatological Problems	Any skin problems (rashes, dermatitis, etc) for a prolonged period of time?
Chronic somatization	Repeated non response to treatment, pattern of recurrent investigations for a number of complaints where nothing comes up
Large medical chart	Tend to be chronic, frequent users of medical system

* Observed and reported behaviour should be incorporated into the evaluation.

12 x5

Appendix B

Anxiety Flowchart

Step 1: Does the patient have the symptoms and signs of Anxiety?

Physical Symptoms
- Palpitations
- Sweating
- "Butterflies" in the stomach
- Shortness of breath
- Nausea/Diarrhea
- "Light headed"
- Tremulous

Psychological Symptoms
- Fear, anxiety, tension, worry, indecision
- Apprehension, startled easily
- Irritability
- Restlessness, poor concentration
- Insomnia

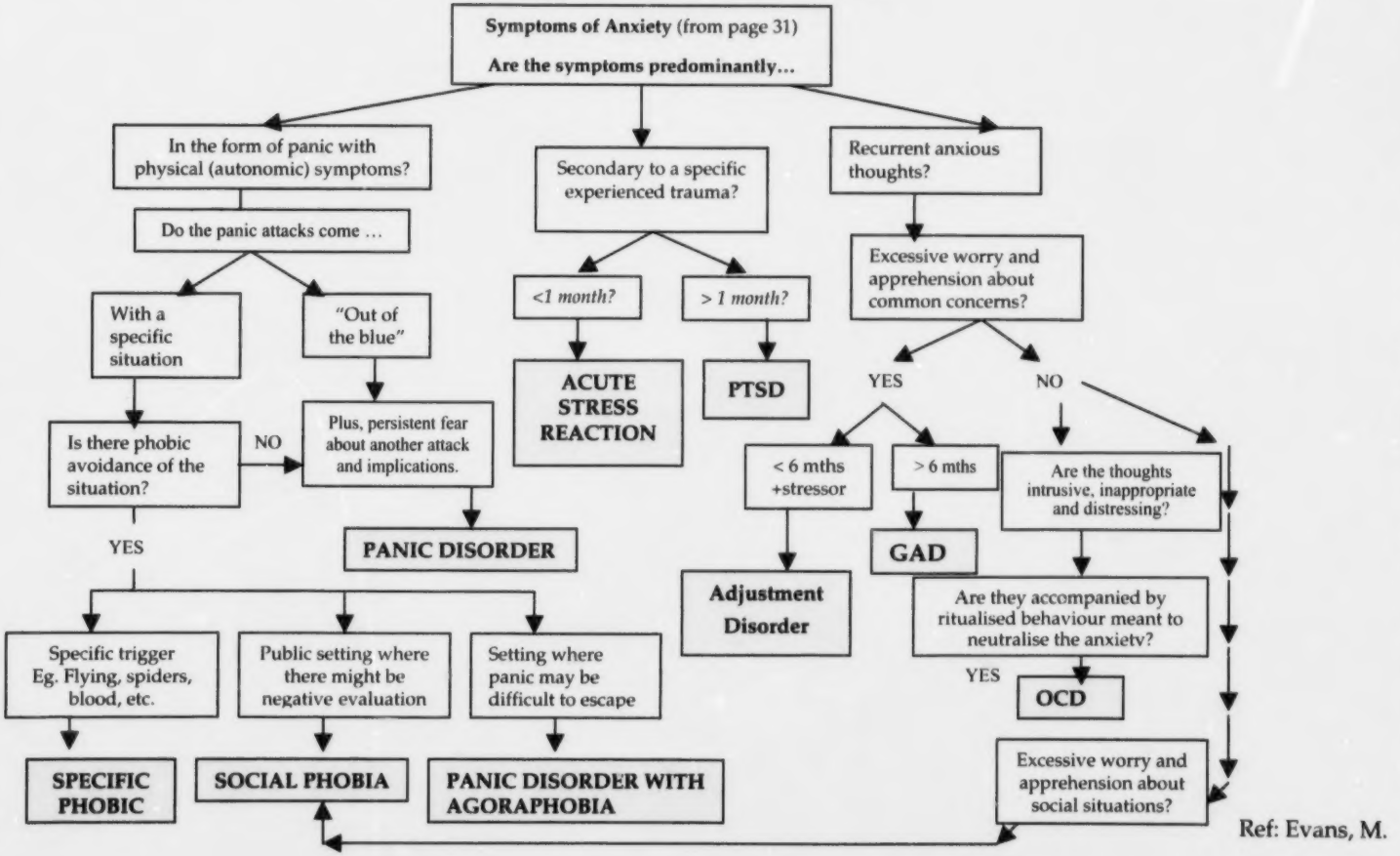
Functional Changes
- Sudden loss to chronic limitation
- Self medicating (e.g., alcohol)
- Avoidance, housebound
- Poor relationships
- High utilization of medical resources

Step 2: Consider and Treat other Causes of Anxiety or Co-morbidities

Diagnosis To Consider	Depression	Substance Abuse
• Hyperthyroidism • Temporal lobe epilepsy • Endocrine dysfunction • Pheochromocytoma • Caffeine abuse • Other stimulants • Cardiac illness	• Considerable overlap in symptoms • Consider isolated depression symptoms such as anhedonia and weight changes • Assess severity and suicidal ideation	• Identify if abusing alcohol and/or drugs • Identify dependence and/or harmful/hazardous use • Educate regarding relationships between substance abuse and anxiety • Initiate treatment plan (ARF phone number for anxiety substance abuse program)

Reference: Evans, M. (2000)

Differentiating Anxiety Disorders


Symptoms of Anxiety (from page 31)
Are the symptoms predominantly...
In the form of panic with physical (autonomic) symptoms?
Secondary to a specific experienced trauma?
Recurrent anxious thoughts?
Do the panic attacks come ...
With a specific situation
"Out of the blue"
<1 month?
> 1 month?
Excessive worry and apprehension about common concerns?
ACUTE STRESS REACTION
PTSD
YES
NO
Is there phobic avoidance of the situation?
NO
Plus, persistent fear about another attack and implications.
< 6 mths +stressor
> 6 mths
Are the thoughts intrusive, inappropriate and distressing?
PANIC DISORDER
YES
GAD
Adjustment Disorder
Are they accompanied by ritualised behaviour meant to neutralise the anxietv?
Specific trigger Eg. Flying, spiders, blood, etc.
Public setting where there might be negative evaluation
Setting where panic may be difficult to escape
YES
OCD
Excessive worry and apprehension about social situations?
SPECIFIC PHOBIC
SOCIAL PHOBIA
PANIC DISORDER WITH AGORAPHOBIA

Ref: Evans, M.

Appendix C

Cognitive-Behavioural Therapy (CBT) Terms[1]

Biofeedback – Involves training patients to be aware of and to change bodily cues that indicate changes in blood pressure, body temperature, and muscle tension.

Breathing Retraining – involves breathing exercises that help control and prevent overbreathing and hyperventilation that can cause breathlessness and lightheadedness associated with anxiety.

Cognitive Restructuring – Involves identifying cognitive distortions (i.e., unrealistic beliefs that contribute to the problem) and changing these beliefs by examining the evidence that supports and contradicts these beliefs.

Exposure (including imaginal exposure) – Involves confronting feared situations repeatedly in a controlled and structured manner until fear has decreased. Exposure may be conducted in vivo or in imagination. Furthermore, exposure based treatments vary with respect to therapist involvement and the rate at which treatment progresses to more difficult situations.

Exposure-Response Prevention (ERP) – Identical to exposure therapy except the person also needs to resist performing his/her compulsive ritual.

Functional Analysis – This consists of an exploration of the environmental variables that maintain a problem behaviour. Functional analysis allows for the development of specific strategies to help the patient change his or her environment so that a more adaptive pattern of behaviour is reinforced.

Homework Assignments – Patients are required to complete specific homework assignments between sessions. Homework may include monitoring the person's reactions, reading about the presenting disorder, practicing specific therapeutic strategies (e.g., exposure to feared situations, challenging cognitive distortions, using specific social skills, relaxation exercises, engaging in specific activities etc).

Hypothesis Testing – Involves testing the validity of the patient's negative predications in specific situations.

Problem Solving Training – Involves teaching patients a series of steps (e.g., identifying problems, generating solutions, evaluating solutions, implementing solution, etc.) to solve problems that come up in everyday life.

Relaxation Training – involves positive thinking, visualization, breathing retraining, and muscle relaxation exercises that help to reduce the general levels of autonomic arousal, improve sleep and relieve some physical symptoms of anxiety (headaches, stomach pain, diarrhea, constipation).

Self-Monitoring – Patients are typically required to monitor relevant feelings, thoughts, and behaviours between therapy sessions. Monitoring forces the patient to be more aware of his or her behaviours and provides the therapist with information necessary for choosing strategies that might be effective for a given patient. On the spot monitoring has the advantage of not being contaminated by retrospective recall biases.

Skills Training- Involves teaching the patient specific strategies to decrease stress and anxiety. Strategies may include assertiveness training, muscle relaxation, imagery, and breathing retraining.

Stress Inoculation Training – involves relaxation training, breathing retraining, positive thinking and self talk, and assertiveness training.

Supportive Psychotherapy – involves developing a strong patient-doctor alliance and making a concerted effort to help the patient solve life problems.

Slow Diaphragmatic Breathing
Below are instructions for slow diaphragmatic breathing. When you first start to practice this technique, you should do so in a quiet room, where you are unlikely to be interrupted. Sit in a comfortable chair and wear clothing that is not constricting. After you have begun to master the technique, you may practice in other locations, including situations that you normally find stressful. Below are some additional instructions to keep in mind.

1. Try to breathe from your abdomen (the lower part of your lungs) as opposed to the chest (the upper part of your lungs).
2. Breathe at a rate of around 8-12 breaths per minute.
3. Inhale a normal volume of air as opposed to large breaths (in other words, try to breathe *slowly* rather than *deeply*).
4. Maintain a smooth inhalation and exhalation cycle (in other words, don't hold your breath after your inhale).
5. As you breathe, count your breaths with each inhalation (e.g., 1, 2, etc.). As you exhale, mentally say the word "relax." After counting 10 breaths, return to "1" and start over.
6. Practice the exercise repeatedly for 10 minutes at a time, at least twice per day.
7. Apply at times of heightened anxiety only after you feel comfortable and skilled in the method of slow diaphragmatic breathing. Apply by spending anywhere from 30 seconds to how ever long you want of slow diaphragmatic breathing.

1. **Reference: Antony MM. 2000.**

Appendix D

Diagnostic Criteria for Anxiety Disorders [1]

1. Reprinted with permission.
American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC, American Psychiatric Association, 1994.

Diagnostic Criteria for Panic Disorder

A. Recurrent unexpected or uncued ***panic attacks*** (see definition below) where at least one of the attacks has been followed by 1 month or more of one (or more) of the following:

- Persistent concern about having additional attacks.
- Worry about the implications of the attack or its consequences (e.g., losing control, having a heart attack, "going crazy").
- A significant change in behaviour related to the attacks.

Panic Attack
A discrete period of intense fear or discomfort, in which four or more of the following symptoms developed abruptly and reached a peak within 10 minutes:

- Palpitations, pounding heart or accelerated heart rate
- Sweating
- Trembling or shaking
- Sensations of shortness of breath or smothering
- Feeling of choking
- Chest pain or discomfort
- Nausea or abdominal distress
- Feeling dizzy, unsteady, lightheaded, or faint
- Feelings of unreality or of being detached from oneself
- Fear of losing control or going crazy
- Fear of dying
- Numbness or tingling sensations
- Chills or hot flashes

B. The presence of ***Agoraphobia:***

Agoraphobia is often an indicator of the severity of an anxiety disorder, typically panic disorder. This leads to the following clinical scenarios:

- Anxiety about being in places or situations from which escape might be difficult or embarrassing, or in which help may not be available in the event of having an unexpected panic attack or panic-like symptoms. Fears typically involve situations that include being outside the home alone, being in a crowd or standing in a line, being on a bridge, and travelling in a bus, train or automobile.
- The situations are avoided or else are endured with marked distress or with anxiety about having a panic attack or panic-like symptoms, or require the presence of a companion.
- The anxiety or phobic avoidance is not better accounted for by another mental disorder, such as Social Phobia (e.g., avoidance limited to social situations), Specific Phobia (e.g., avoidance limited to a single situation like elevators), or Obsessive-Compulsive Disorder (e.g., avoidance of dirt in someone with a contamination obsession).

C. The panic attacks are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hyperthyroidism).

D. The panic attacks are not better accounted for by another mental disorder.

Diagnostic Criteria for Social Phobia (Social Anxiety Disorder)

A. A marked or persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. The individual fears that he or she will act in a way (or show anxiety symptoms) that will be humiliating or embarrassing.

B. Exposure to the feared social situation almost invariably provokes anxiety, which may take the form of a situationally bound or situationally predisposed panic attack.

C. The person usually recognizes that the fear is excessive or unreasonable.

D. The feared social or performance situations are avoided or else are endured with intense anxiety or distress.

E. The avoidance, anxious anticipation, or distress in the feared social situation(s) interferes significantly with the person's normal routine, occupational (academic) functioning, or social activities or relationships, or there is marked distress about having the phobia.

F. In individuals under age 18 years, the duration is at least 6 months.

G. The fear or avoidance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition and is not better accounted for by another mental disorder (e.g., panic disorder with or without agoraphobia, separation anxiety disorder, body dismorphic disorder, a pervasive developmental disorder, or schizoid personality disorder).

H. If a general medical condition or another mental disorder is present, the fear in criterion A is unrelated to it, e.g., the fear is not of stuttering, trembling in Parkinson's disease, or exhibiting abnormal eating behaviour in anorexia nervosa or bulimia nervosa.

Specify if **Generalized:** if fears include most social situations (e.g., initiating or maintaining conversations, participating in small groups, dating, speaking to authority figures, attending parties.)

Diagnostic Criteria for Specific Phobia

A. Marked and persistent fear that is excessive or unreasonable cued by the presence or anticipation of a specific object or situation (e.g., flying, heights, animals, receiving an injection, seeing blood).

B. Exposure to the phobic stimulus almost invariably provokes an immediate anxiety response, which may take the form of a situationally predisposed panic attack. Note: In children, the anxiety may be expressed by crying, tantrums, freezing or clinging.

C. The person recognizes that the fear is excessive or unreasonable. Note: In children, this feature may be absent.

D. The phobic stimuli or situation(s) is avoided or else is endured with intense anxiety.

E. The avoidance or anxious anticipation or distress in the feared situation(s) interferes significantly with the person's normal routine, occupational or academic functioning, or social activities or relationships, or there is marked distress about having the phobia.

F. In individuals under age 18 years, the duration is at least 6 months.

G. The anxiety, Panic Attacks or phobic avoidance associated with the specific object or situation are not better accounted for by another mental disorder, such as Obsessive-Compulsive Disorder (e.g., fear of dirt in someone with an obsession about contamination), Separation Anxiety Disorder (e.g., avoidance of school), Social Phobia (e.g., avoidance of social situations because of fear of embarrassment), or Panic Disorder.

Specify Type:

Animal Type: if animals or insects cue the fear. Generally has a childhood onset.

Natural Environment Type: objects in the natural environment (e.g., heights, storms, water) cue the fear. Generally has a childhood onset.

Blood-Injection-Injury Type: the fear is cued by seeing blood or an injury or by receiving an injection or other invasive medical procedure. This subtype tends to run in families and is often characterized by a strong vasovagal response and fainting. Phobia of hospitals, physicians and medical procedures can lead to avoidance and non-compliance. This type of anxiety is difficult to detect since these patients tend to avoid the medical system.

Situational Type: fear is cued by a specific situation such as elevators, flying, driving or enclosed places. There are two peak onset ages, one in childhood and another in the mid-20s. This subtype appears to be similar to Panic Disorder with Agoraphobia in its characteristic sex ratios, familial aggregation pattern and age at onset.

Other Type: if the fear is cued by other stimuli including fear or avoidance of situations that may lead to choking, vomiting, or contracting an illness; "space" phobia (i.e., the individual is afraid of falling down if away from walls or other means of physical support); and children's fears of loud sounds or costumed characters.

Diagnostic Criteria for Generalized Anxiety Disorder

(Includes Overanxious Disorder of Childhood)

A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work, health, finances or school performance).

B. The person finds it difficult to control the worry.

C. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms present for more days than not for the past 6 months). **Note:** only one item is required in children.
   - restlessness or feeling keyed up or on edge
   - being easily fatigued
   - difficulty concentrating or mind going blank
   - irritability
   - muscle tension
   - sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep)

D. The focus of the anxiety and worry is not confined to features of an Axis I disorder; e.g., the anxiety or worry is not about having a Panic Attack (as in panic Disorder), being embarrassed in public (as in Social Phobia), being contaminated (as in Obsessive-Compulsive Disorder), gaining weight (as in Anorexia Nervosa) having multiple physical complaints (as in Somatization Disorder) or having a serious illness (as in Hypochondriasis), and the anxiety and worry do not occur exclusively during Posttraumatic Stress Disorder.

E. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning.

F. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hyperthyroidism) and does not occur exclusively during a Mood Disorder, a Psychotic disorder, or a Pervasive Developmental disorder.

Diagnostic Criteria for Post-Traumatic Stress Disorder

A. Occurs in individuals who have been exposed to a traumatic event (e.g., combat, sexual abuse/rape, natural disasters) in which both of the following were present:
(1) the person experienced, witnessed or was confronted with an event(s) that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others.
(2) the person's response involved intense fear, helplessness, or horror. Note: In children, this may be expressed instead as disorganized or agitated behaviour.

B. The traumatic event is persistently experienced in one (or more) of the following ways:
- recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions. Note: In young children, repetitive play may occur in which themes or aspects of the trauma are expressed.
- recurrent distressing dreams of the event. Note: In children, there may be frightening dreams without recognizable content.
- acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and dissociative flashback episodes, including those that occur on awakening or when intoxicated). Note: In young children, trauma-specific reenactment may occur.
- intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event.
- physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event.

C. Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three (or more) of the following:
- efforts to avoid thoughts, feelings or conversations associated with the trauma
- efforts to avoid activities, places, or people that arouse recollections of the trauma
- inability to recall an important aspect of the trauma
- markedly diminished interest or participation in significant activities
- feeling of detachment or estrangement from others
- restricted range of affect (e.g., unable to have loving feelings)
- sense of a foreshortened future (e.g., does not expect to have a career, marriage, children, or a normal life span)

D. Persistent symptoms of increased arousal (not present before the trauma), as indicated by two (or more) or the following:
- difficulty falling or staying asleep
- irritability or outbursts of anger
- difficulty concentrating
- hypervigilance
- exaggerated startle response

E. Duration of the disturbance (symptoms in Criteria B, C and D) is more than 1 month.

F. The disturbance causes clinically significant distress or impairment in social, occupational or other important areas of functioning.

Specify **Acute** if duration of symptoms is < 3 months or **Chronic** if duration of symptoms > 3 months.
Specify **With Delayed Onset** if onset of symptoms is at least 6 months after the stressor.

Diagnostic Criteria for Acute Stress Disorder

A. The person has been exposed to a traumatic event in which both of the following were present:
   (1) the person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others
   (2) the person's response involved intense fear, helplessness, or horror

B. Either while experiencing or after experiencing the distressing event, the individual has three or more of the following dissociative symptoms:
   (1) a subjective sense of numbing, detachment, or absence of emotional responsiveness
   (2) a reduction in awareness of his or her surroundings (e.g., "being in a daze")
   (3) derealization
   (4) depersonalization
   (5) dissociative amnesia (i.e., inability to recall an important aspect of the trauma)

C. The traumatic event is persistently reexperienced in at least one of the following ways: recurrent images, thoughts, dreams, illusions, flashback episodes, or a sense of reliving the experience; or distress on exposure to reminders of the traumatic event.

D. Marked avoidance of stimuli that arouse recollections of the trauma (e.g., thoughts, feelings, conversations, activities, places, people).

E. Marked symptoms of anxiety or increased arousal (e.g., difficulty sleeping, irritability, poor concentration, hypervigilance, exaggerated startle response, motor restlessness).

F. The disturbance causes clinically significant distress or impairment in social, occupational or other important areas of functioning or impairs the individual's ability to pursue some necessary task, such as obtaining necessary assistance or mobilizing personal resources by telling family members about the traumatic experience.

G. The disturbance lasts for a minimum of 2 days and a maximum of 4 weeks and occurs within 4 weeks of the traumatic event.

H. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition, is not better accounted for by Brief Psychotic Disorder, and is not merely an exacerbation of a preexisting Axis I or Axis II disorder.

Diagnostic Criteria for Obsessive-Compulsive Disorder

A. Either obsessions or compulsions.

Obsessions as defined by:

- recurrent and persistent thoughts, impulses or images that are experienced, at some time during the disturbance, as intrusive and inappropriate and that cause marked anxiety or distress
- the thoughts, impulses, or images are not simply excessive worries about real-life problems
- the patient attempts to ignore or suppress such thought, impulses, or images, or to neutralize them with some other thought or action
- the person recognizes that the obsessive thoughts, impulses, or images are a product of his or her own mind (not imposed from without as in thought insertion)

Compulsions as defined by:

- repetitive behaviours (e.g., hand washing, ordering, checking) or mental acts (e.g., praying, counting, repeating words silently) that the person feels driven to perform in response to an obsession, or according to rules that must be applied rigidly
- the behaviours or mental acts are aimed at preventing or reducing distress or preventing some dreaded event or situation; however, these behaviours or mental acts either are not connected in a realistic way with what they are designed to neutralize or prevent or are clearly excessive

B. At some point during the course of the disorder, the person has recognized that the obsessions or compulsions are excessive or unreasonable. Note: This does not apply to children.

C. The obsessions or compulsions cause marked distress, are time consuming (take more than 1 hour a day), or significantly interfere with the person's normal routine, occupation or academic functioning, or usual social activities or relationships.

D. If another disorder is present, the content of the obsessions or compulsions is not restricted to it (e.g., preoccupation with food in the presence of an Eating Disorder; hair pulling in the presence of Trichotillomania; concern with appearance in the presence of Body Dysmorphic Disorder; preoccupation with drugs in the presence of a Substance Use Disorder; preoccupation with having a serious illness in the presence of Hypochondriasis; preoccupation with sexual urges or fantasies in the presence of a Paraphilia; or guilty ruminations in the presence of Major Depressive Disorder).

E. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Specify **With Poor Insight** if, for most of the time during the current episode, the person does not recognize that the obsessions and compulsions are excessive or unreasonable.

Appendix E

Pharmacotherapy Summary

Anxiolytic Summary

Drug Class	Comments
Benzodiazepines **(BZD)**	• Useful for Panic Disorder, Social Phobia, and GAD • BDZs considered 'targeted substances' in Canada as of Sept. 2000. Refills must be specified at time of ordering prescription and only one pharmacy transfer allowed. • Evidence for efficacy, but first line use is not recommended except as an adjunct during onset of treatment • More rapid acting than other medications or psychosocial therapy • Withdrawal reactions, rebound and relapse effects associated with discontinuation[1,2,3] • Potential to interfere with the patient's ability to respond to cognitive-behavioural therapy and to deal with underlying issues • Can interfere with the ability to drive and increase the risk of falls in the elderly
Buspirone (Buspar®)	• Helpful for treating GAD • Produces less drowsiness and psychomotor impairment than BZD • Does not potentiate the effects of alcohol • No psychological dependence; no withdrawal issues • Requires 3 to 5 weeks for maximal effectiveness and may have lower response rates in patients with a history of BZD use. • Not cross-tolerant with benzodiazepines

1. Withdrawl- Symptoms occur 1-2 days (short acting) to 5-10 days (long-acting) following drug discontinuation. Symptoms of withdrawl include insomnia, agitation, anxiety, perceptual changes, dysphoria and GI distress.
2. Rebound- Symptoms occur hours to days after drug withdrawl. Symptoms of anxiety are similar but more intense than original symptoms
3. Relapse- Symptoms occur weeks to months after drug withdrawl and are similar to original symptoms of anxiety.

Therapeutic Tips for Using Benzodiazepines

- ***Limited role in therapy***

  Avoid using BZDs as first line therapy because of risk of abuse, but don't exclude them as an option since there are some people that do very well with them.

  May be useful as short-term adjunct during onset of treatment, since faster onset of action than SSRIs and tricyclics.

  Useful as an alternative if a patient hasn't done well on other medications. For example, a short term, low dose BZD is a reasonable alternative where other strategies have failed in situational anxiety.

  PRN use is not recommended. Unfortunately there is limited evidence about the risk/benefit of taking patients off low dose chronic BZDs. Up to 40% of participants in small surveys responded to a letter of invitation to decrease or discontine BZD use.

- ***Lowest effective dose and shortest period of time***
  Higher dose or longer period increases chances of seeing withdrawal issues and side effects. Even in 2 to 3 weeks the patient may experience rebound symptoms.

- ***Avoid use or use with extreme caution where previous alcohol or drug abuse issues exist. Do not co-prescribe with barbiturates, TCAs or other BZDs.***

- ***Discuss risk of sedation especially when initiating treatment (driving vehicles, using machinery, drug interactions)***

- ***Caution in elderly; increases risk of falls and hip fractures four fold (if alcohol is involved this becomes 10 fold)***

- ***Management of BZD Withdrawal (see also Appendix E)***
  Taper over 2 to 3 months if patient on BZD for an extended period of time
  Note that relapse rates are higher if only BZD have been used over a long term.
  CBT can be useful for helping patients get off BZD.

Managing Benzodiazepine Discontinuation

Principles of Benzodiazepine Discontinuation

1. Benzodiazepines should never be abruptly stopped in patients with long-term use, unless life-threatening complications warrant immediate discontinuation. Patients who have been taking benzodiazepines for short periods or using them intermittently do not require tapering.
2. Discontinuation from benzodiazepines should be slow and gradual.

Problems with discontinuing benzodiazepines are primarily the result of the frequent occurrence of withdrawal anxiety and recurrence of the original symptoms:

Common	Uncommon	Serious
Rebound anxiety	Perceptual disturbances	Psychosis
Insomnia	Tinnitus	Delirium
GI distress		Seizures

- Make sure the patient understands the benefits of cessation.

- **Graded reduction of current benzodiazepine** is best undertaken in those who take only benzodiazepines and have become dependent while taking doses within the therapeutic range. The dose may be tapered at a rate of approximately 10-15% per week of the current dose (not original) over 6-12 week. In patients who have been on benzodiazepine for many years, tapering could take even longer.

- **Substitution of a long-acting benzodiazepine** if the benzodiazepine has a short half-life (<15h) consider substituting with an equivalent dose of an agent with a longer half-life (e.g., diazepam), which is easier to discontinue. Substitution of a long-acting benzodiazepine allows a more gradual reduction of dose with fewer withdrawal symptoms.

- It is suggested that patients be converted to an equivalent daily dose of the new agent but be allowed to use their current benzodiazepine p.r.n. if not enough of the substituted benzodiazepine is given.

Benzodiazepine Equivalence

Drug	Equivalence to 5 mg diazepam (mg)
Alprazolam (Xanax®)	0.5*
Bromazepam (Lectopam®)	3
Chlordiazepoxide (Librium®)	25
Clonazepam (Rivotril®)	0.25
Clorazepate (Tranxene®)	10
Diazepam (Valium®)	5
Flurazepam (Dalmane®)	15
Lorazepam (Ativan®)	1
Nitrazepam (Mogadon®)	2.5
Oxazepam (Serax®)	15
Temazepam (Restoril®)	10
Triazolam (Halcion®)	0.25*

*equivalency uncertain

Adapted from: Kalvik A, Issac P, Janecek E. Benzodiazepines: treatment of anxiety, insomnia and alcohol withdrawal. Pharmacy Connection 1995; Sept/Oct: 20-32.

- It should be noted that equivalencies are approximate. If the patient reports over-sedation on the new medication, the dose should be lowered; if the patient reports significant withdrawal symptoms, the dose may be increased.

- The patient should be stabilized prior to initiating the taper process. Use a gradual tapering schedule over the course of 6 to 12 weeks (10-20% decrease from current dose every 3 to 5 days), although some patients may require a longer tapering schedule. The key to successfully discontinuing benzodiazepine therapy is to work with the patient to define goals and design the tapering schedule. The first 50% of the dose can be reduced relatively rapidly, however, the next 25% should be reduced more slowly and the final 25% should be reduced most slowly and cautiously. **Allow for flexibility**. The percentage decrease and duration of taper will vary considerably amongst individuals. If a decrement is not tolerated, quickly return to the previous dose, stabilize, then continue the taper more gradually.

- Offer regular support sessions. Patients should be encountered to note positive effects of the taper, such as feeling more alert and energetic. Patients should be reminded that in some cases withdrawal symptoms may be unavoidable no matter how slow the taper.

- Be certain that the patient is not substituting alcohol for the benzodiazepine. An effort should be made in speaking to family members to obtain more information.

- If this approach is unsuccessful, continue to provide medication and supportive therapy with the option of another attempt at withdrawal in the future.

Management of High Dose Benzodiazepine Withdrawal

- Patients using benzodiazepines in a dose equivalent to diazepam 50 mg/day or higher risk seizures, psychosis, or delirium if their dose is stopped abruptly. The risk is greater with use of benzodiazepines with a short half-life.
- Patients taking between 50 to 80 mg per day of diazepam or equivalent should receive inpatient care if possible, but they can be treated as outpatients if they are medically and psychiatrically stable, are not combining benzodiazepines with other substances such as alcohol or opioids, and are reliable and unlikely to access benzodiazepines from the street and other doctors.
- Daily dispensing is suggested.
- If typical daily use over the past 2 months is equivalent to diazepam 100 mg or more, consider hospitalization and addiction medicine consult.

Clonazepam or Diazepam tapering for Benzodiazepine Withdrawal

Outpatient protocol:	• Convert to equivalent dose of diazepam (maximum 80-100 mg/day) in divided doses • Taper by 5 mg per week (or 5 mg per 3-4 days at doses above 50 mg) • Adjust initial dose and rate of taper according to symptoms • Slow taper at doses below 20 mg • Allow for flexibility

M121

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Antidepressant Summary

Drug Class	Comments
SSRIs (Selective Serotonin Reuptake Inhibitors) Fluoxetine **(Prozac®)** Fluvoxamine **(Luvox®)** Paroxetine **(Paxil®)** Sertraline **(Zoloft®)** Citalopram **(Celexa®)**	• Useful for most types of anxiety problems (except specific phobias) • Generally recommended first line due to a better side effect profile • Caution in elderly particularly when used with another drug with sedative or hypnotic properties such as a benzodiazepine.
SNRI (Serotonin Norepinephrine Reuptake Inhibitor) Venlafaxine **(Effexor®)**	• Evidence is lacking except in panic disorder and generalized anxiety disorder • Similar adverse effects to SSRIs • At higher doses can also cause a dose dependent increase in diastolic blood pressure
Tricyclic and Related Antidepressants Clomipramine **(Anafranil®)**	• Most useful for people affected by panic disorder and Obsessive-Compulsive Disorder (OCD) • Effective in post-traumatic stress disorder and generalized anxiety disorder • Avoid in patients with incomplete/ complete heart block • Caution in elderly due to their anticholinergic and antiadrenergic effects which may cause constipation, dry mouth and eyes, delirium and orthostatic hypotension
Desipramine **(Norpamin®)** Imipramine **(Tofranil®)**	• Not useful for OCD, social phobia, or specific phobia • Effective for panic disorder, post-traumatic stress disorder and generalized anxiety disorder • Avoid in patients with incomplete/ complete heart block • Caution in elderly due to their anticholinergic and antiadrenergic effects which may cause constipation, dry mouth and eyes, delirium and orthostatic hypotension.
MAOI (Monoamine Oxidase Inhibitors) Phenelzine **(Nardil®)** Tranylcypromine **(Parnate®)**	• Helpful for most disorders, but are often not preferred agents because of the necessary dietary restrictions of tyramine-containing foods to avoid hypertensive crisis. • Not useful for specific phobia
RIMA (Reversible Monoamine Oxidase Inhibitors) Moclobemide **(Manerix®)**	• Does not require adherence to a tyramine free diet at usual doses. • In social phobia some trials indicate a benefit, however in other trials the efficacy is questionable.
SARI (Serotonin Antagonist Receptor Inhibitors) Nefazodone **(Serzone®)**	• Useful in panic disorder • Similar adverse effects to SSRIs • Effective antidepressant but little efficacy in most anxiety disorders.
NDM (Norepinephrine Dopamine Modulator) Bupropion **(Wellbutrin SR®)**	• Effective antidepressant but may not be as effective in anxiety disorders

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Switching to Another Antidepressant

There is little evidence about the best strategy for selecting a second antidepressant if the first is not tolerated or not effective. For the newer antidepressants, switching to an antidepressant of the same class may be effective, especially if the second agent offers a better side effect profile. For some patients, switching to an antidepressant of another class may be more helpful.

The following table summarizes the recommended washout period when switching from one antidepressant to another. When no washout is required, good clinical practice recommends tapering and stopping one antidepressant before starting the next medication. In situations where time is important, the next medication can usually be started and increased gradually while tapering the old medication.

Discontinuing Antidepressants

Caution is advised when stopping antidepressants because discontinuation reactions have been reported. Symptoms may include dizziness, nausea, paresthesia and headache and generally appear within the first few days of abrupt withdrawal.[1] Because of a longer half-life, fluoxetine (Prozac) discontinuation is less likely to result in these symptoms.

The following suggestions should be considered to minimize discontinuation effects:

- Avoid abrupt discontinuation and/or 'drug holidays'.
- Reassure that symptoms are generally mild and transient.
- Taper all SSRIs except fluoxetine and sertraline(long half-life).
- The final dose should be less than the initial minimum therapeutic dose.
- Reinitiate the original agent and slow the tapering rate if symptoms are intolerable.
- Consider giving a single dose of fluoxetine (20 mg) if unable to discontinue original SSRI.

Reference: Lynn MacDonald. Discontinuation reactions associated with SSRIs. Canadian Adverse Drug Reaction Newsletter: Therapeutic Products Programme. October 1998.

1. Mneumonic for antidepressant discontinuation symptoms:
   F lu-like symptoms
   I nsomnia
   N ausea
   I mbalance
   S ensory disturbances
   H yper-arousal (anxiety/agitation)

Switching Anti-depressants

Switching from:	Switching to						
	SSRI	SARI	SNRI	NDM	TCA	RIMA	MAOI
SSRI **Fluoxetine** **Fluvoxamine** **Paroxetine** **Sertraline** **Citalopram**	**No Washout** Be aware of additive serotonergic effects for up to 1 week after stopping SSRI (5 weeks for fluoxetine)	**No Washout** Be aware of additive serotonergic effects for up to 1 week after stopping SSRI (5 weeks for fluoxetine)	**No Washout**	**No Washout**	**No Washout** Be aware that SSRIs can increase serum TCA levels for up to 1 week after stopping SSRI (5 weeks for fluoxetine)	**1 week (5 weeks for fluoxetine)** Some data indicate that an SSRI & RIMA can be safely combined, but this requires specialist input.	**1 week (5 weeks for fluoxetine)**
SARI **Nefazodone**	**No Washout**	**No Washout**	**No Washout**	**No Washout**	**No Washout**	**1 week**	**1 week**
SNRI **Venlafaxine** **Venlafaxine XR**	**No Washout**	**No Washout**	**N/A**	**No Washout** Bupropion should be started at a lower dose to avoid additive norardrenergic effects	**No Washout** TCA should be started at a lower dose to avoid additive noradrenergic effects	**1 week**	**1 week**
NDM **Bupropion SR**	**No Washout**	**No Washout**	**No Washout** Venlafaxine should be started at a lower dose to avoid additive noradrenergic effects	**N/A**	**No Washout** TCA should be started at a lower dose to avoid additive noradrenergic effects	**No Washout**	**1 week**
TCA **Nortriptyline** **Desipramine** **Imipramine** **Amitriptyline** **and others**	**No Washout** Be aware that SSRI can increase serum levels of TCAs for up to 1 week after stopping TCA. Be aware of additive serotonergic effects when switching from clomipramine to SSRIs.	**No Washout**	**No Washout** Venlafaxine should be started at a lower dose to avoid additive noradrenergic effects	**No Washout** Bupropion should be started at a lower dose to avoid additive noradrenergic effects	**No Washout**	**1 week**	**1 week**
RIMA **Moclobemide**	**3 days**	**3 days**	**3 days**	**3 days**	**3 days**	**N/A**	**3 days**
MAOI **Phenelzine** **Tranylcypromine**	**2 weeks**	**2 weeks**	**2 weeks**	**2 weeks**	**2 weeks**	**2 weeks**	**2 weeks**

Adapted from MacDonald, 1998.

Switching Anti-depressants

Switching from:	Switching to						
	SSRI	SARI	SNRI	NDM	TCA	RIMA	MAOI
SSRI **Fluoxetine** **Fluvoxamine** **Paroxetine** **Sertraline** **Citalopram**	**No Washout** Be aware of additive serotonergic effects for up to 1 week after stopping SSRI (5 weeks for fluoxetine)	**No Washout** Be aware of additive serotonergic effects for up to 1 week after stopping SSRI (5 weeks for fluoxetine)	**No Washout**	**No Washout**	**No Washout** Be aware that SSRIs can increase serum TCA levels for up to 1 week after stopping SSRI (5 weeks for fluoxetine)	**1 week (5 weeks for fluoxetine)** Some data indicate that an SSRI & RIMA can be safely combined, but this requires specialist input.	**1 week (5 weeks for fluoxetine)**
SARI **Nefazodone**	**No Washout**	**No Washout**	**No Washout**	**No Washout**	**No Washout**	**1 week**	**1 week**
SNRI **Venlafaxine** **Venlafaxine XR**	**No Washout**	**No Washout**	**N/A**	**No Washout** Bupropion should be started at a lower dose to avoid additive norardrenergic effects	**No Washout** TCA should be started at a lower dose to avoid additive noradrenergic effects	**1 week**	**1 week**
NDM **Bupropion SR**	**No Washout**	**No Washout**	**No Washout** Venlafaxine should be started at a lower dose to avoid additive noradrenergic effects	**N/A**	**No Washout** TCA should be started at a lower dose to avoid additive noradrenergic effects	**No Washout**	**1 week**
TCA **Nortriptyline** **Desipramine** **Imipramine** **Amitriptyline** **and others**	**No Washout** Be aware that SSRI can increase serum levels of TCAs for up to 1 week after stopping TCA. Be aware of additive serotonergic effects when switching from clomipramine to SSRIs.	**No Washout**	**No Washout** Venlafaxine should be started at a lower dose to avoid additive noradrenergic effects	**No Washout** Bupropion should be started at a lower dose to avoid additive noradrenergic effects	**No Washout**	**1 week**	**1 week**
RIMA **Moclobemide**	**3 days**	**3 days**	**3 days**	**3 days**	**3 days**	**N/A**	**3 days**
MAOI **Phenelzine** **Tranylcypromine**	**2 weeks**	**2 weeks**	**2 weeks**	**2 weeks**	**2 weeks**	**2 weeks**	**2 weeks**

Adapted from MacDonald, 1998.

Frequency of Adverse Reactions to Antidepressants at Therapeutic Doses

Antidepressant	Anticholinergic Effects					CNS Effects					
	Dry Mouth	Blurred Vision	Constipation	Sweating	Delayed Micturition *	Drowsiness, Sedation	Insomnia	Excitement, Hypomania**	Disorientation, Confusion	Headache	Asthenia, Fatigue
Amitriptyline	4	3	3	3	2	4	2	1	3	2	3
Clomipramine	4	3	3	3	2	2	3	1	2	2	2
Desipramine	3	2	2	2	-	2	2	2	-	1	2
Doxepin	4	3	3	2	1	4	2	1	1	1	2
Imipramine	4	3	3	3	3	3	3	3	2	3	3
Nortriptyline	3	2	3	1	1	2	1	2	3	1	3
Protriptyline	3	3	3	3	1	1	3	3	-	-	3
Trimipramine	3	2	3	2	1	4	2(b)	1	3	2	2
Amoxapine	4	2	4	2	3	3	3	2	2	2	2
Maprotiline	4	3	3	2	2	3	1	2	2	1	-
Phenelzine	4	3	3	2	2	3	3(c)	3	2	2	1
Tranylcypromine	3	2	2	-	2	3	3(c)	3	2	-	1
Moclobemide	3	3	2	2	1	2	3(c)	2	2	3	1
Fluoxetine	3	2	2	2	2	3	3(c)	3	3	3	3
Fluvoxamine	3	2	3	3	2	3	3	3	2	3	3
Paroxetine	3	2	3	3	2	3	3	2	1	3	3
Sertraline	3	2	2	2	1	3	3	3	1	3	2
Netazodone	3	3	3	2	1	3	2	2	3	3	3
Trazodone	3	2(a)	2	-	1	4	2	-(d)	1	2	3
Venlafaxine	3	2	3	3	1	3	3(c)	3	2	3	3
Bupropion+	3	3	3	3	2	2	3	3	2	3	2

1 = <2%, 2 = >2%, 3 = >10%, 4 = >30%, - None reported in literature perused. * Primarily in the elderly, ** More likely in bipolar patients.
(a) Found to lower intraocular pressure, (b) No effect on REM sleep, (c) Especially if given in the evening, (d) Less likely to precipitate mania.
Adapted from: Butler K, Jeffries J. Clinical Handbook of Psychotropic Drugs, 9th Edition.
+ Information refers to immediate release form of bupropion.

Frequency of Adverse Reactions to Antidepressants at Therapeutic Doses cont...

Antidepressant	Extrapyramidal Effects		Cardiovascular Effects				Other Effects				
	Unspecified	Tremor	Orthostatic Hypotension, Dizziness	Tachycardia, palpitations	ECG Changes***	Cardiac Arrhythmia	GI Distress	Dermatitis Rash	Weight Gain (over 6 kg)	Sexual Disturbances	Epileptic Seizures****
Amitriptyline	2(e)	3	3	3	3(i)	2	2	2	4	2	1
Clomipramine	1(e)	3	3	3	3(i)	2	3	2	3	4	1(p)
Desipramine	1	2	2	3	2(i)	2	1	1	3	2	1
Doxepin	2(e)	2	3	2	2(i)	2	1	1	3	2	1
Imipramine	1	3	4	3	3(i)	2	3	2	3	4	1
Nortriptyline	-	3	2	2	2(i)	2	1	1	2	1	1
Protriptyline	-	2	3	2	3(i)	2	-	1	1	1	1
Trimipramine	1	3	3	2	3(i)	2	1	1	3	1	1
Amoxapine	2(e)	2	3	3	1(i)	1	2	3	1	2	1(p)
Maprotiline	2	3	2	2	1(i)	1	2	3	3	1	2(p)
Phenelzine	3	3	3	3(h)	1(j)	1	3	1	3	4(n)	1
Tranylcypromine	1	2	3	3(h)	2(j)	1	2	2	2	2(n)	-(q)
Moclobemide	1	2	3	2	2	2	3	2	1	1	1
Fluoxetine	2(e)	3	3	1(h)	1	1(k)	3	2	1(m)	4(n)	1
Fluvoxamine	2	3	2	1(h)	1	1	4	2	1(m)	4	1
Paroxetine	2	3	3	2(h)	1	1	3	1	2(m)	4(n)	1
Sertraline	2	3	3	2(h)	1	1	4	2	1(m)	4(n)	1
Nefazodone	1	1	3	1(h)	1	1	3	1	1	1	1
Trazodone	2(e)	2	3(f)	2	2	2(l)	3	1	2	1(n)	1
Venlafaxine	2	2	3(g)	2	1	1	4	2	1(m)	4	1
Bupropion+	2	3	2(g)	2	1	1	3	2	1(m)	1(n,o)	1(r)

1 = <2%, 2 = >2%, 3 = >10%, 4 = >30%, - None reported in literature perused. *** ECG Abnormalities usually without cardiac injury. **** In non-epileptic patients, risks increased with elevated plasma levels. (e) Tardive dyskinesia reported (rarely). (f) Less frequent if drugs given after meals. (g) Hypertension reported. (h) Decreased heart rate reported. (i) Conduction delays: increased PR, QRS or QT interval. (j) Shortened QT interval. (k) Slowing of sinus node and atrial dysrhythmia. (l) Patients with pre-existing cardiac disease have a 10% incidence of premature ventricular contractions. (m) Weight loss reported. (n) Priapism reported. (o) Improved sexual functioning. (p) Higher incidence if dose above 250 mg daily of clomipramine, 300 mg daily of amoxapine or 225 mg daily of maprotiline (q) May have anticonvulsant activity (r) Higher incidence if dose above 450 mg daily or in patients with Bulimia Nervosa. Information refers to immediate release form of bupropion.

Adapted from Butler K, Jefferies J. Clinical Handbook of Psychotropic Drugs, 9th Edition.

Frequency of Adverse Reactions to Antidepressants at Therapeutic Doses

Antidepressant	Anticholinergic Effects					CNS Effects					
	Dry Mouth	Blurred Vision	Constipation	Sweating	Delayed Micturition *	Drowsiness, Sedation	Insomnia	Excitement, Hypomania**	Disorientation, Confusion	Headache	Asthenia, Fatigue
Amitriptyline	4	3	3	3	2	4	2	1	3	2	3
Clomipramine	4	3	3	3	2	2	3	1	2	2	2
Desipramine	3	2	2	2	-	2	2	2	-	1	2
Doxepin	4	3	3	2	1	4	2	1	1	1	2
Imipramine	4	3	3	3	3	3	3	3	2	3	3
Nortriptyline	3	2	3	1	1	2	1	2	3	1	3
Protriptyline	3	3	3	3	1	1	3	3	-	-	3
Trimipramine	3	2	3	2	1	4	2(b)	1	3	2	2
Amoxapine	4	2	4	2	3	3	3	2	2	2	2
Maprotiline	4	3	3	2	2	3	1	2	2	1	-
Phenelzine	4	3	3	2	2	3	3(c)	3	2	2	1
Tranylcypromine	3	2	2	-	2	3	3(c)	3	2	-	1
Moclobemide	3	3	2	2	1	2	3(c)	2	2	3	1
Fluoxetine	3	2	2	2	2	3	3(c)	3	3	3	3
Fluvoxamine	3	2	3	3	2	3	3	3	2	3	3
Paroxetine	3	2	3	3	2	3	3	2	1	3	3
Sertraline	3	2	2	2	1	3	3	3	1	3	2
Nefazodone	3	3	3	2	1	3	2	2	3	3	3
Trazodone	3	2(a)	2	-	1	4	2	-(d)	1	2	3
Venlafaxine	3	2	3	3	1	3	3(c)	3	2	3	3
Bupropion+	3	3	3	3	2	2	3	3	2	3	2

1 = <2%, 2 = >2%, 3 = >10%, 4 = >30%, - None reported in literature perused. * Primarily in the elderly, ** More likely in bipolar patients.
(a) Found to lower intraocular pressure, (b) No effect on REM sleep, (c) Especially if given in the evening, (d) Less likely to precipitate mania.
Adapted from: Butler K, Jeffries J. Clinical Handbook of Psychotropic Drugs, 9th Edition.
+ Information refers to immediate release form of bupropion.

Frequency of Adverse Reactions to Antidepressants at Therapeutic Doses cont...

Antidepressant	Extrapyramidal Effects		Cardiovascular Effects				Other Effects				
	Unspecified	Tremor	Orthostatic Hypotension, Dizziness	Tachycardia, palpitations	ECG Changes***	Cardiac Arrhythmia	GI Distress	Dermatitis Rash	Weight Gain (over 6 kg)	Sexual Disturbances	Epileptic Seizures****
Amitriptyline	2(e)	3	3	3	3(i)	2	2	2	4	2	1
Clomipramine	1(e)	3	3	3	3(i)	2	3	2	3	4	1(p)
Desipramine	1	2	2	3	2(i)	2	1	1	3	2	1
Doxepin	2(e)	2	3	2	2(i)	2	1	1	3	2	1
Imipramine	1	3	4	3	3(i)	2	3	2	3	4	1
Nortriptyline	-	3	2	2	2(i)	2	1	1	2	1	1
Protriptyline	-	2	3	2	3(i)	2	-	1	1	1	1
Trimipramine	1	3	3	2	3(i)	2	1	1	3	1	1
Amoxapine	2(e)	2	3	3	1(i)	1	2	3	1	2	1(p)
Maprotiline	2	3	2	2	1(i)	1	2	3	3	1	2(p)
Phenelzine	3	3	3	3(h)	1(j)	1	3	1	3	4(n)	1
Tranylcypromine	1	2	3	3(h)	2(j)	1	2	2	2	2(n)	-(q)
Moclobemide	1	2	3	2	2	2	3	2	1	1	1
Fluoxetine	2(e)	3	3	1(h)	1	1(k)	3	2	1(m)	4(n)	1
Fluvoxamine	2	3	2	1(h)	1	1	4	2	1(m)	4	1
Paroxetine	2	3	3	2(h)	1	1	3	1	2(m)	4(n)	1
Sertraline	2	3	3	2(h)	1	1	4	2	1(m)	4(n)	1
Nefazodone	1	1	3	1(h)	1	1	3	1	1	1	1
Trazodone	2(e)	2	3(f)	2	2	2(l)	3	1	2	1(n)	1
Venlafaxine	2	2	3(g)	2	1	1	4	2	1(m)	4	1
Bupropion+	2	3	2(g)	2	1	1	3	2	1(m)	1(n,o)	1(r)

1 = <2%, 2 = >2%, 3 = >10%, 4 = >30%, - None reported in literature perused. *** ECG Abnormalities usually without cardiac injury, **** In non-epileptic patients; risks increased with elevated plasma levels. (e) Tardive dyskinesia reported (rarely), (f) Less frequent if drugs given after meals, (g) Hypertension reported, (h) Decreased heart rate reported, (i) Conduction delays: increased PR, QRS or QT, interval, (j) Shortened QT, interval, (k) Slowing of sinus node and atrial dysrhythmia, (l) Patients with pre-existing cardiac disease have a 10% incidence of premature ventricular contractions, (m) Weight loss reported, (n) Priapism reported, (o) Improved sexual functioning, (p) Higher incidence if dose above 250 mg daily of clomipramine, 300 mg daily of amoxapine or 225 mg daily of maprotiline (q) May have anticonvulsant activity (r) Higher incidence if dose above 450 mg daily or in patients with Bulimia Nervosa. + Information refers to immediate release form of bupropion.

Adapted from Butler K, Jefferies J. Clinical Handbook of Psychotropic Drugs, 9th Edition.

Appendix F

Consumer and Self-Help Reading List

Reference: Antony, MM. 2000.

Panic Disorder and Agoraphobia

Craske, MG, & Barlow, DH (2000). *Mastery of your anxiety and panic, third edition (MAP 3) (client workbook and client workbook for agoraphobia).* San Antonio TX: The Psychological Corporation.

Otto MW, Pollack MH, Barlow DH (1996). *Stopping anxiety medication: panic control therapy for benzodiazepine discontinuation (client workbook).* San Antonio, TX: The Psychological Corporation.

Wilson RR (1996). *Don't panic: Taking control of anxiety attacks.* New York: Harper Perennial.

Zuercher-White E (1997). *An end to panic: Breakthrough techniques for overcoming panic disorder,* 2nd edition. Oakland, CA: New Harbinger Publications.

Specific Phobias

Antony MM, Craske MG, Barlow DH (1995). *Mastery of your phobia (client workbook).* San Antonio TX: The Psychological Corporation.

Bourne EJ (1998). *Overcoming specific phobia: A hierarchy and exposure-based protocol for the treatment of all specific phobias (client manual).* Oakland, CA: New harbinger Publications.

Brown D (1996). *Flying without fear.* Oakland, CA: New Harbinger Publications.

Hartman C, Huffaker JS (1995). *The fearless flyer: How to fly in comfort and without trepidation.* Portland, OR: Eighth Mountain Press.

Social Phobia

Antony, MM, & Swinson, RP (2000). *The shyness and social anxiety workbook: Proven, step-by-step techniques for overcoming your fear.* Oakland, CA: New Harbinger Publications.

Franks H (1996). *Hidden fears: Self help for anxiety and phobias.* London: Headline Book Publishing.

Markway BG, Carmin CN, Pollard CA, Flynn T (1992). *Dying of embarrassment: help for social anxiety and phobia.* Oakland, CA: New Harbinger Publications.

Rapee RM (1998). *Overcoming shyness and social phobia: A step-by-step guide.* Northvale, NJ: Jason Aronson.

General Anxiety, Stress and Depression

Bourne EJ (1995). *The anxiety and phobia workbook*, 2nd edition. Oakland, CA: New Harbinger Publications.

Butler G, Hope T (1995). *Managing your mind: The mental fitness guide*. New York, NY: Oxford University Press.

Davis M, Eshelman ER, McKay M (1995). *The relaxation and stress reduction workbook*, fourth edition. Oakland, CA: New Harbinger Publications.

Greenberger D, Padesky CA (1995). *Mind over mood: A cognitive therapy treatment manual for clients*. New York: Guilford Press.

Johnson S (1997). *Taking the anxiety out of tests: A step-by-step guide*. Oakand, CA: New Harbinger Publications.

McKay M, Davis M, Fanning P (1997). *Thoughts and feelings: Taking control of your moods and your life*, second edition. Oakland, CA: New Harbinger Publications.

Post-Traumatic Stress Disorder

Matsakis A (1996). *I can't get over it: A handbook for trauma survivors*, 2nd edition. Oakland, CA: New Harbinger Publications.

Obsessive-Compulsive Disorder

Foa EB, Kozak MJ (1997). *Mastery of your obsessive compulsive disorder, client workbook*. San Antonio, TX: The Psychological Corporation.

Foa EB, Wilson R (1991). *Stop obsessing! How to overcome your obsessions and compulsions*. New York: Bantam Books.

Hyman BM, Pedrick C (1999). *The OCD workbook: Your guide to breaking free from obsessive-compulsive disorder*. Oakland, CA: New Harbinger Publications.

Neziroglu F, Yaryura-Tobias JA (1991). *Over and over again*. Lexington, MA: DC Heath and Company.

Schwartz JM (1996). *Brainlock: Free yourself from obsessive-compulsive behavior*. New York: Regan Books.

Steketee GS (1999). *Overcoming obsessive compulsive disorder (client manual)*. Oakland, CA: New Harbinger Publications.

Sources for books on the reading list

1. New Harbinger Publications (Available from the publisher and from some bookstores.)
   5674 Shattuck Avenue, Oakland, CA 94609
   1-800-748-6273
2. Psychological Corporation
   Not available in bookstores. Must be ordered from the Psychological Corporation.
   In Canada, Harcourt Brace and Company: 1-800-387-7278 or (416) 255-4491

Bookstores with excellent self-help selections: Chapters & Indigo Books – various locations

Appendix G

Practical Treatment Manuals for Clinicians*

Panic Disorder

Craske, MG, & Barlow, DH (2000). *Mastery of your anxiety and panic, third edition (MAP 3) (client workbook and client workbook for agoraphobia).* San Antonio TX: The Psychological Corporation

Otto MW, Jones JC, Craske MG, Barlow DH (1996). *Stopping anxiety medication: panic control therapy for benzodiazepine discontinuation (therapist guide).* San Antonio, TX: The Psychological Corporation.

Zuercher-White E (1997). *Treating panic disorder and agoraphobia: A step by step clinical guide.* Oakland, CA: New Harbinger Publications.

Social Phobia

Hope DA, Heimberg RG, Juster H and Turk CL (2000). *Managing social anxiety: a cognitive-behavioral therapy approach (Client workbook).* San Antonio, TX: The Psychological Corporation.

Rapee RM, Sanderson WC (1998). *Social phobia: Clinical application of evidence-based psychotherapy.* Northvale, NJ: Jason Aronson.

Scholing A, Emmelkamp PMG, Van Oppen P (1996). Cognitive-behavioral treatment of social phobia. In VB Van Hasselt, M. Hersen (Eds.) *Sourcebook of psychological treatment manuals for adult disorders.* New York: Plenum Press.

Specific Phobia

Antony MM, Barlow DH (1998). Specific phobia. In VE Caballo (Ed.), *Handbook of cognitive behavioural treatments for psychological disorders.* Exeter, UK Elvesier.

Craske MG, Antony MM, Barlow DH (1997). *Mastery of your specific phobia, therapist guide.* San Antonio, TX: The Psychological Corporation.

Generalized Anxiety Disorder

Brown TA, O'Leary TA, Barlow DH (1993). Generalized anxiety disorder. In DH Barlow (Ed.), *Clinical handbook of psychological disorders,* second edition. New York: Guilford Press.

Obsessive-Compulsive Disorder

Kozak MJ, Foa EB (1997). *Mastery of your obsessive compulsive disorder, therapist guide.* San Antonio, TX: The Psychological Corporation.

Steketee GS (1999). *Overcoming obsessive compulsive disorder* (therapist protocol). Oakland, CA: New Harbinger Publications.

Post-Traumatic Stress Disorder

Ballenger JC, Davidson JR, Lecrubier Y, et al. Consensus statement on posttraumatic stress disorder from the International Consensus Group on Depression and Anxiety. J Clin Psychiatry 2000;61 Suppl 5:60-6

Calhoun KS, Resick PA (1993). Post-traumatic stress disorder. In DH Barlow (Ed.). *Clinical handbook of psychological disorders*, second edition. New York: Guilford Press.

Foa EB, Rothbaum BO (1998). *Treating the trauma of rape: Cognitive behavioural therapy for PTSD*. New York, NY: Guilford.

Other Treatment Manuals

Andrews G., Crino R., Hunt C., Lampe L., & Page A. (1994). *The treatment of anxiety disorders: Clinician's guide and patient manuals*. New York, NY: Cambridge University Press.

Antony M.M., & Swinson R.P. (2000). *Phobic disorders and panic in adults: A guide to assessment and treatment*. Washington, DC: American Psychological Association.

Wells A. (1997). Cognitive therapy of anxiety disorders: A practice manual and conceptual guide. New York, NY: John Wiley and Sons.

Benzodiazepine Dependence and Withdrawal

Busto UE, Sykora K, Sellers EM. A clinical scale to assess benzodiazepine withdrawal. J Clin Psychoppharmacology 1989; 9 (6): 412-416.

Rickels K, DeMartinis N, Rynn M, et al. Pharmacologic strategies for discontinuing benzodiazepine treatment. J Clin Psycopharmacology 1999; 19(6) suppl 2: 12S-16S.

* The guideline panel would like to acknowledge Dr. Martin Antony's contribution to developing these appendices.

Appendix H

Video Resources

Clark DM (1998). *Cognitive therapy for panic disorder (video tape).* APA Psychotherapy Videotape Series. Washington, DC: American Psychological Association.

Padesky C. *Testing automatic thoughts with thought records (video tape).* Oakland, CA: New Harbinger Publications.

Rapee RM (1999). *Fight or flight? Overcoming panic and agoraphobia (video tape).* New York, NY: Guilford Publications.

Rapee RM (1999). *I think they think...Overcoming social phobia (video tape).* New York, NY: Guilford Publications.

Turner SM (1998). *Behavior therapy for OCD (video tape).* Washington, DC: American Psychological Association.

Appendix I

Anxiety Related Associations

Anxiety Disorders Association of America
11900 Parklawn Drive, Suite 100
Rockville, MD 20852
Tel: (301) 231-9350
Fax: (301) 231-7392
Email: anxdis@aol.com
Web Page: www.adaa.org

- Newsletter
- Information on support groups in the United States and Canada
- Names of professionals who treat anxiety disorders in the United
- States and Canada
- Book catalog

OC Foundation
P.O. Box 70
Milford, CT 06460
Tel: (203) 878-5669
Fax: (203) 874-2826
Email: jphs28a@prodigy.com
Web Page: http://pages.prodigy.com/alwillen/ocf.html

- Newsletter
- Information on self-help groups
- Book catalogue

Appendix J

Internet Resources

Agoraphobia Resource Page
www.cstone.net/users/maybell/agora.htm

Anxieties.com
www.anxieties.com/home.htm

Anxiety and Panic Book Store
members.aol.com/healthbook/stress

Anxiety-Panic.com (internet links)
anxiety-panic.com/default.cfm

Anxiety and Panic Internet Resource
www.algy.com/anxiety/index.html

Anxiety Disorders Association of America
www.adaa.org

Anxiety Disorders and their Treatment: A Critical Review of the Evidence-Based Literature, by M.M. Antony and R.P. Swinson (Health Canada, 1996)
www.hc-sc.gc.ca/hppb/mentalhealth/pdfs/anxiety_review.pdf

Anxiety Disorders Cyberpsych Penpals
www.userhome.com/cyberpsych/penpals

Anxiety Network International
www.anxietynetwork.com

Anxiety Relief Center (Bristol-Myers Squibb)
www.anxiety-relief.com

Canadian Network for Mood and Anxiety Treatments (CANMAT)
www.canmat.org

CBT Website
www.cognitivetherapy.com

DIRECT – Anxiety Information Centre
www-fhs.mcmaster.ca/direct/anxiety/anxiety.html

Doctors Guide to Anxiety Disorders Information and Resources
www.pslgroup.com/anxiety.htm

Fear of Flying
www.anxieties.com/7Flying/summary.htm

Fear of Flying
www1.nb.sympatico.ca/healthyway/HEALTHYWAY/feature_fly1.html

Internet Mental Health
www.mentalhealth.com

National Anxiety Foundation
www.lexington-on-line.com/naf.html

NIMH Anxiety Disorders Education Program
www.nimh.nih.gov/anxiety

Obsessive Compulsive Anonymous
members.aol.com/west24th/index.html

Obsessive Compulsive Disorder
www.fairlite.com/ocd/

Obsessive Compulsive Disorder
www.kidsource.com/kidsource/content/obsess.html#top

OCD Central
www.geocities.com/HotSprings/5403/index.html

OCD Resource Center
www.ocdresource.com

OC Foundation
pages.prodigy.com/alwillen/ocf.html

Paxil Anxiety Disorders Page
www.panicattack.com

Shyness Home Page
www.shyness.com

Social Phobia / Social Anxiety Association
www.socialphobia.org

Social Anxiety Network
www.social-anxiety-network.com

Spider Homepage (excellent exposure materials for people with spider phobias)
www.powerup.com.au/~glen/spideri.htm

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